On the Positive Steady States of Deficiency-One Mass Action Systems

Balázs Boros

Ph.D. Thesis

Supervisor: György Michaletzky, professor, D.Sc.

Doctoral School of Mathematics
Director: Miklós Laczkovich

Doctoral Program of Applied Mathematics
Director: György Michaletzky

Department of Probability Theory and Statistics, Institute of Mathematics,
Faculty of Science, Eötvös Loránd University, Budapest, Hungary

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Introduction

The foundations of Chemical Reaction Network Theory (CRNT) was developed by Feinberg, Horn, and Jackson in the 1970's [25, 26, 31, 32, 38, 39, 40, 41, 42, 43]. The aim of the theory is to investigate the qualitative properties of the mathematical models of chemical and biological systems. The most studied model is the so-called *mass action system*, which is a continuous-time continuous-state deterministic model, where the state of the system is the concentrations of the chemical species involved (examples of chemical species are H_2, O_2, and H_2O), and the state varies in time in accordance with an autonomous ordinary differential equation (ODE). The main objects of the model are the directed graph $(\mathcal{C}, \mathcal{R})$, called the *graph of complexes* (the elements of $\mathcal{C}$ are certain linear combinations of the species and the element of $\mathcal{R}$ are the reactions, e.g. once the reaction $2H_2 + O_2 \to 2H_2O$ takes place in the model, we have $2H_2 + O_2, 2H_2O \in \mathcal{C}$ and $(2H_2 + O_2, 2H_2O) \in \mathcal{R}$) and the *rate coefficients* (a positive number appearing in the ODE as a multiplier is assigned to all reactions). Despite the several parameters in the model, there are powerful results concerning the qualitative behaviour of these systems.

In the past decade, a renewed attention has been paid to the understanding of biological phenomena such as multistability or periodic behaviour. Recent works were focusing on the persistence, the boundedness of the trajectories, and global stability of such systems [1, 2, 3, 4, 5, 6, 17, 45, 53]. Also, much effort has been dedicated to addressing the question of (ruling out) multiple equilibria [7, 8, 18, 19, 20]. The paper [21] investigates both the existence and the uniqueness of positive steady states.

In this thesis, we revisit and improve the *deficiency-oriented* theory developed by Feinberg, Horn, and Jackson. The deficiency, denoted by δ, is a nonnegative integer associated to the *reaction network* under consideration. The classical Deficiency-Zero- and Deficiency-One Theorems answer questions about the existence, uniqueness, and stability properties of the steady states. The main purpose of this thesis is to investigate the existence of steady states of such deficiency-one mass action systems that do not satisfy the assumptions of the Deficiency-One Theorem.

The rest of this thesis is organised as follows. After a brief chapter on notations, we provide an introduction to the basic notions of CRNT in Chapter 2. In Chapter 3, we recall some known results about the set of positive steady states (i.e., the steady states of the ODE with all coordinates being positive) of mass action systems for which the deficiency of the underlying reaction network satisfies $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$, where δ^1, $\delta^2, \ldots, \delta^\ell$ denote the deficiencies of the subnetworks of the original network associated to the weak components of the graph of complexes, which, of course, are reaction networks themselves. Still in Chapter 3, we prove under $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$ that the non-emptiness of the set of positive steady states is equivalent to the non-emptiness of the set of positive steady states of all the subsystems associated to the weak components of the graph of complexes. This result is also known, but the proof we present is new and shows the way we search for positive steady states. It will be apparent that our approach makes it possible to extend the classical Deficiency-One Theorem.

In Chapter 4, we recall the Deficiency-Zero- and Deficiency-One Theorems. Though these are, again, known results, we still prove them in order to demonstrate that the deficiency-one case can be treated in the same way as the deficiency-zero case, provided that a not CRNT-specific result (which we also present in details) is available. It was not apparent from the CRNT literature so far that the deficiency-one case is only slightly more complicated than the deficiency-zero case. As a consequence of this clarification, we were also able to extend the Deficiency-One Theorem. The classical result of Feinberg states that if the graph of complexes is strongly connected and the deficiency equals to one then the set of positive steady states is nonempty (regardless of the value of the rate coefficients). We also treat in Chapter 4 the case when the graph of complexes is weakly connected, but not strongly connected and the deficiency equals to one. It turns out that a trivially obtained necessary condition also serves as a sufficient condition to the non-emptiness of the set of positive steady states. Thus, we make the Deficiency-One Theorem complete in respect of the existence of the positive steady states. Chapter 4 is based on [11] and [12].

In CRNT, a reaction network is called *weakly reversible* if all the weak components of the graph of complexes are strongly connected. In Chapter 5, we prove the existence of a positive steady state for every weakly reversible deficiency-one mass action systems (regardless of the values of the rate coefficients). It turned out that independently of our work, Deng, Feinberg, Jones, and Nachman obtained the same conclusion without any assumption on the deficiency (see the yet unpublished manuscript [23]). Thus, their result is substantially more general. The tools in the two works are completely different. Most of the intermediate results in [23] rely heavily on the weak reversibility of the network, while in our reasoning the weak reversibility of the network becomes crucial only in the concluding steps. Rather, we take advantage of the fact that the deficiency of the network is assumed to be one. Thus, the results in Chapter 5 might also contribute to the theory of those deficiency-one mass action systems that are *not* weakly reversible, but significant additional ideas are needed for that. Chapter 5 is based on [14].

The equivalent condition we obtain in Chapter 4 for the non-emptiness of the set of positive steady states (for deficiency-one mass action systems with weakly connected, but not strongly connected graph of complexes) involves the rate coefficients. As it will be demonstrated by examples, three different kind of phenomena can occur for such reaction networks when rate coefficients are assigned to the network:

- the set of positive steady states is *nonempty* for the resulting mass action system for all rate coefficients,

- the set of positive steady states is *empty* for the resulting mass action system for all rate coefficients, and
- the non-emptiness of the set of positive steady states for the resulting mass action system *depends on the rate coefficients* (i.e., there exist rate coefficients such that the set of positive steady states is nonempty for the resulting mass action system and there also exist rate coefficients such that the set of positive steady states is empty for the resulting mass action system).

In Chapter 6, we provide characterisations of these phenomena. Thus, given a deficiency-one reaction network with weakly connected, but not strongly connected graph of complexes, one can decide which of the above three statements holds. We use graph theoretical terms and arguments throughout this thesis, but Chapter 6 is certainly the most involved in this respect. Chapter 6 is based on [13].

There follows a few general remarks by the author. Beside the presentation of my new CRNT-results, it was also my intension to provide a comprehensive proof of the Deficiency-One Theorem. Particularly, I intended to separate the results that are rather graph theoretic ones from those that are CRNT-specific. Also, the reason behind the creation of a separate chapter on mass action systems with $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$ was to emphasise that several arguments used in the proof of the Deficiency-Zero- and Deficiency-One Theorems are not specifically related to the fact that the deficiency is small. Similarly, there are a few CRNT-specific, but not at all deficiency-related statements we make use of while proving the Deficiency-Zero- and Deficiency-One Theorems.

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Chapter 1

Notations

Denote by $\mathbb{R}$ and $\mathbb{Z}$ the set of real and integer numbers, respectively. For $p, q \in \mathbb{Z}$ let

$$\overline{p,q} = \{k \in \mathbb{Z} \mid p \leq k \leq q\}.$$

The function $\operatorname{sgn} : \mathbb{R} \to \{-1, 0, 1\}$ is the sign function (i.e., $\operatorname{sgn}(x) = 1$ for $x > 0$, $\operatorname{sgn}(x) = -1$ for $x < 0$, and $\operatorname{sgn}(0) = 0$).

We denote by $\mathbb{R}_+$ and $\mathbb{R}_{\geq 0}$ the sets of positive and nonnegative real numbers, respectively, i.e.,

$$\mathbb{R}_+ = \{x \in \mathbb{R} \mid x > 0\} \text{ and } \mathbb{R}_{\geq 0} = \{x \in \mathbb{R} \mid x \geq 0\}.$$

The sets $\mathbb{R}^p_+$ and $\mathbb{R}^p_{\geq 0}$ are called the *positive* and *nonnegative orthants* of $\mathbb{R}^p$, respectively. For $v \in \mathbb{R}^p$, the ith coordinate of v is denoted by v_i ($i \in \overline{1,p}$). For $A \in \mathbb{R}^{p \times q}$, the jth column and the (i,j)th entry of A are denoted by $A_{\cdot j}$ and A_{ij}, respectively ($i \in \overline{1,p}$, $j \in \overline{1,q}$). For a matrix A, denote by $\ker A$, $\operatorname{ran} A$, $\operatorname{rank} A$, and $A^\top$ its kernel, range, rank, and transpose, respectively. For a square matrix A, denote by $\det A$ the determinant of A.

For a vector space V, denote by $\dim V$ its dimension. For the linear subspaces $V_1, V_2, \ldots, V_k$ of a vector space V, the notation $V = V_1 \oplus V_2 \oplus \cdots \oplus V_k$ expresses that V is the direct sum of $V_1, V_2, \ldots, V_k$ (i.e., for each $v \in V$ there exists a unique $(v_1, v_2, \ldots, v_k) \in V_1 \times V_2 \times \cdots \times V_k$ such that $v = v_1 + v_2 + \cdots + v_k$). For subsets $V_1, V_2, \ldots, V_k$ of a vector space V, the linear subspace of V, generated by the sets $V_1, V_2, \ldots, V_k$, is denoted by $\operatorname{span}(V_1, V_2, \ldots, V_k)$.

The functional $\langle \cdot, \cdot \rangle : \mathbb{R}^p \times \mathbb{R}^p \to \mathbb{R}$ denotes the standard scalar product on $\mathbb{R}^p$ (i.e., $\langle x, y \rangle = \sum_{i=1}^p x_i y_i$ for $((x,y) \in \mathbb{R}^p \times \mathbb{R}^p)$). For a subspace V of $\mathbb{R}^p$, denote by $V^\perp$ the orthogonal complement of V (i.e., $V^\perp = \{x \in \mathbb{R}^p \mid \langle x, y \rangle = 0 \text{ for all } y \in V\}$).

For a set $A \subseteq \mathbb{R}^p$, the boundary of A is denoted by $\operatorname{bd}(A)$.

The kth derivative of a k times differentiable function g is denoted by $\partial^k g$, while the ith partial derivative of g is denoted by $\partial_i g$ (or by $\partial_x g$ in case the ith variable of g is denoted by x).

Let us agree in the convention that if $w \in \mathbb{R}^p_+$ for some positive integer p then $\log(w) \in \mathbb{R}^p$

is the vector, which is obtained by taking the natural logarithm of w coordinatewise, i.e.,

$$\log(w) = \begin{bmatrix} \log(w_1) \\ \log(w_2) \\ \vdots \\ \log(w_p) \end{bmatrix} \in \mathbb{R}^p.$$

We do not indicate the number p in the notation $\log(w)$, it is implicitly indicated by knowing the dimension of w.

For any finite set X, $X_0 \subseteq X$, and function $g : X \to \mathbb{R}$ we define $g(X_0)$ by

$$g(X_0) = \sum_{x \in X_0} g(x). \tag{1.1}$$

We make this convention in order to ease the notation in several situations.

For any set A, denote the cardinality of A by $|A|$.

We also summarise here the graph theoretical notations that will be used throughout this thesis. For more details on these, please refer to Appendix A. Let $D = (V, A)$ be a directed graph for the rest of this chapter. For $i, j \in V$, the set of directed paths from i to j is denoted by $\overrightarrow{i, j}$. For a directed path P we denote by $V[P]$ the vertex set of P (we use the notation $V[P]$ even if the vertex set of the directed graph in question is denoted by some other symbol than V) and by $\operatorname{len}(P)$ the length of P. For $i_1, i_2, i_3 \in V$, $P \in \overrightarrow{i_1, i_2}$, and $Q \in \overrightarrow{i_2, i_3}$, denote by $\operatorname{con}(P, Q)$ the concatenation of P and Q.

For $U \subseteq V$ let us denote by $\varrho_D^{\text{in}}(U)$ and $\varrho_D^{\text{out}}(U)$ set of arcs that enter U and leave U, respectively. For a function $z : A \to \mathbb{R}$, denote by excess_z the excess function associated to D and z. For $i \in V$ we use the notations $\varrho^{\text{in}}(i)$, $\varrho^{\text{out}}(i)$, and $\text{excess}_z(i)$ instead of $\varrho^{\text{in}}(\{i\})$, $\varrho^{\text{out}}(\{i\})$, and $\text{excess}_z(\{i\})$, respectively. For $U \subseteq V$, denote by $\mathcal{T}_D(U)$ the set of U-branchings in D. Finally, for $i, j \in V$ and $U \subseteq V$ let us define $\mathcal{T}_D^{ij}(U)$ by

$$\mathcal{T}_D^{ij}(U) = \{\widetilde{A} \in \mathcal{T}_D(U) \mid \text{there exists a directed path from } i \text{ to } j \text{ in } (V, \widetilde{A})\}.$$

Chapter 2

Basic notions from Chemical Reaction Network Theory

In this chapter we summarise the basic notions from CRNT that are used throughout this thesis. Most of these notions were introduced by Feinberg, Horn, and Jackson. See e.g. [27] or [29] for a more detailed introduction than the one in this chapter.

2.1 Chemical reaction networks

Consider a nonempty finite set of *chemical species*, denoted by $\mathcal{X}$. Let $n = |\mathcal{X}|$ and denote the chemical species by the symbols $X_1, X_2, \ldots, X_n$. Thus, $\mathcal{X} = \{X_1, X_2, \ldots, X_n\}$.

A *chemical complex* is a linear combination of the species with nonnegative integer coefficients (e.g. $X_1 + 3X_2 + 2X_4$). These nonnegative integer coefficients are called the *stoichiometric coefficients*. The complex with all stoichiometric coefficients being zero is called the *zero complex* (see [27, Section 4] for the practical utility of allowing the zero complex in the model). The set of chemical complexes, denoted by $\mathcal{C}$, is assumed to be a nonempty finite set. Let $c = |\mathcal{C}|$ and denote the chemical complexes by the symbols $C_1, C_2, \ldots, C_c$. Thus, $\mathcal{C} = \{C_1, C_2, \ldots, C_c\}$. In order to ease the notation, we use the notations $i \in \mathcal{C}$ and $C_i \in \mathcal{C}$ interchangeably ($i \in \overline{1,c}$).

The set of *reactions*, denoted by $\mathcal{R}$, is a nonempty subset of

$$\{(C_i, C_j) \in \mathcal{C} \times \mathcal{C} \mid i, j \in \overline{1,c}, i \neq j\}.$$

Thus, a reaction is an ordered pair of distinct complexes. For further reference, let $m = |\mathcal{R}|$. If $(C_i, C_j) \in \mathcal{R}$ for some $i, j \in \overline{1,c}$ then we say that C_i is the *reactant complex* and C_j is the *product complex* of the reaction. We assume that each complex takes part in at least one reaction, i.e., there does not exist $C_i \in \mathcal{C}$ such that $\mathcal{R} \subseteq (\mathcal{C} \backslash \{C_i\}) \times (\mathcal{C} \backslash \{C_i\})$. We mostly write $(i, j) \in \mathcal{R}$ instead of $(C_i, C_j) \in \mathcal{R}$ ($i, j \in \overline{1,c}$).

We are now in the position to tell what we mean by a chemical reaction network.

Definition 2.1 *A* chemical reaction network *(*reaction network *or* network *for short) is a triple $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ of three nonempty finite sets, where $\mathcal{X}$ is the set of chemical species, $\mathcal{C}$ is the set of* *chemical complexes, and $\mathcal{R}$ is the set of reactions as described above.*

We remark that usually another mild assumption is made, namely that for all species there exists a complex such that the stoichiometric coefficient of the species in that complex is positive. However, it is more convenient not to make this assumption in this thesis, because if we do not make this assumption then it is possible to consider a subnetwork of the network with the same set of species as the original one. This plays a role e.g. in Chapter 3.

The following example of a reaction network will be used throughout this chapter for illustrative purposes. Let the set of species $\mathcal{X}$, the set of complexes $\mathcal{C}$, and the set of reactions $\mathcal{R}$ be

$$\mathcal{X} = \{X_1, X_2, X_3, X_4, X_5\}, \tag{2.1}$$

$$\mathcal{C} = \{C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8\}, \text{ and} \tag{2.2}$$

$$\mathcal{R} = \{(1,2),(2,1),(2,3),(3,4),(4,3),(4,1),(5,6),(6,7),(7,8),(8,5)\}, \tag{2.3}$$

respectively, where

$$\begin{array}{llll} C_1 = X_1 + X_2, & C_2 = 2X_2, & C_3 = 2X_4, & C_4 = X_3 + X_4, \\ C_5 = X_1 + 3X_5, & C_6 = X_2, & C_7 = X_4, & C_8 = X_1 + X_3. \end{array} \tag{2.4}$$

Note that in this example we have $n = 5$, $c = 8$, and $m = 10$. Mostly, reaction networks are given by their *reaction schemes*. The reaction scheme of the reaction network $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ defined by (2.1)-(2.4) is

$$\begin{tikzcd} X_1 + X_2 \arrow[r, shift left] & 2X_2 \arrow[l, shift left] \arrow[d] & X_1 + 3X_5 \arrow[r] & X_2 \arrow[d] \\ X_3 + X_4 \arrow[u] \arrow[r, shift left] & 2X_4 \arrow[l, shift left] & X_1 + X_3 \arrow[u] & X_4. \arrow[l] \end{tikzcd} \tag{2.5}$$

A convenient way to specify the set of complexes is to provide an $n \times c$ matrix, denoted by B, whose entries are nonnegative integers, the rows refer to the species, and the columns refer to the complexes. The matrix B is called the *matrix of complexes*. Using the introduced terminology, B_{si} is then the stoichiometric coefficient of the species X_s in complex C_i ($s \in \overline{1,n}, i \in \overline{1,c}$). We remark that all the statements and proofs in this thesis remain valid without any change if the stoichiometric coefficients take their values from the set $\{0\} \cup [1, \infty)$, i.e., if $B \in (\{0\} \cup [1, \infty))^{n \times c}$.

For the reaction network in (2.5), the matrix of complexes is

$$B = \begin{bmatrix} 1 & 0 & 0 & 0 & 1 & 0 & 0 & 1 \\ 1 & 2 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 2 & 1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 3 & 0 & 0 & 0 \end{bmatrix} \in \mathbb{R}^{5 \times 8}.$$

2.2 Mass action systems

In the sequel, we introduce the kinetic differential equation associated to a chemical reaction network $(\mathcal{X}, \mathcal{C}, \mathcal{R})$. Let us represent by the vector $x(\tau) \in \mathbb{R}^n$ the *concentrations* of the species at time τ. Thus, the sth coordinate of $x(\tau)$, $x_s(\tau)$, represents the concentration of the species X_s at time τ ($s \in \overline{1,n}$). A continuous-time continuous-state deterministic model will be considered, where the species concentrations are changing in accordance with the autonomous ordinary differential equation (ODE)

$$\dot{x}(\tau) = \sum_{(i,j)\in\mathcal{R}} \kappa_{(i,j)} \prod_{s=1}^{n} |x_s(\tau)|^{B_{si}} \cdot (B_{\cdot j} - B_{\cdot i}) \tag{2.6}$$

with state space $\mathbb{R}^n$, where $(\kappa_{(i,j)})_{(i,j)\in\mathcal{R}}$ are given positive real numbers, called the *rate coefficients* (in the sequel, we mostly write κ_{ij} instead of $\kappa_{(i,j)}$). Since the state space of (2.6) is the open set $\mathbb{R}^n$, there exists a unique solution for (2.6) on a maximal open interval for all initial values (since $B_{si} \in \{0\} \cup [1, \infty)$ for all $s \in \overline{1,n}$ and for all $i \in \overline{1,c}$, the function on the right hand side of (2.6) is locally Lipschitz continuous). As (2.6) describes the evolution of species concentrations, we are interested in solutions with initial values in the nonnegative orthant $\mathbb{R}^n_{\geq 0}$. Both the nonnegative orthant ($\mathbb{R}^n_{\geq 0}$) and the positive orthant ($\mathbb{R}^n_{+}$) are forward invariant sets for (2.6). Proof of this well-known fact can be found e.g. in [57, Section 2], [58, Chapter 12], [54, Section VII], or [10, Section 6.1]. This means that the mathematical model under consideration satisfies the qualitative property that no species concentration can become negative. Thus, we will consider (2.6) with state space $\mathbb{R}^n_{\geq 0}$ in the sequel, and also, we omit the absolute value sign in notation.

The purpose of CRNT is to provide qualitative results concerning the solutions of (2.6). Clearly, once we are given a chemical reaction network $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ and a *rate coefficient function* $\kappa : \mathcal{R} \to \mathbb{R}_+$, the equation (2.6) is determined.

Definition 2.2 *The quadruple* $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ *is called a* mass action system*, where the triple* $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *is a chemical reaction network and* $\kappa : \mathcal{R} \to \mathbb{R}_+$ *is the rate coefficient function assigned to that.*

The main object we will be interested in in this thesis is the *set of positive steady states*, denoted by E_+, defined by

$$E_+ = \left\{ x \in \mathbb{R}^n_+ \;\middle|\; \sum_{(i,j)\in\mathcal{R}} \kappa_{ij} \prod_{s=1}^{n} x_s^{B_{si}} \cdot (B_{\cdot j} - B_{\cdot i}) = 0 \right\}. \tag{2.7}$$

In order to associate a mass action system to (2.5), one needs to provide the positive real numbers $\kappa_{12}, \kappa_{21}, \kappa_{23}, \kappa_{34}, \kappa_{43}, \kappa_{41}, \kappa_{56}, \kappa_{67}, \kappa_{78}$, and κ_{85}.

In many cases it is more convenient to have another equivalent expressions for (2.6). We introduce these in the next section.

2.3 Other forms of the differential equation

It will be useful in the sequel if another form of (2.6) is also available. To this end, we next introduce the objects I_κ, I, Θ, and R.

Though we have not mentioned it explicitly so far, it is apparent that the ordered pair $(\mathcal{C}, \mathcal{R})$ is a directed graph, and accordingly the triple $(\mathcal{C}, \mathcal{R}, \kappa)$ is a labelled directed graph. It is standard in graph theory to associate to a labelled directed graph a matrix, called the *Laplacian*. (The conventions we use here for the Laplacian are the ones that suits our purposes from the point of view of CRNT.) Let us extend the function $\kappa : \mathcal{R} \to \mathbb{R}_+$ to $\mathcal{C} \times \mathcal{C}$ such that $\kappa_{ij} = 0$ for $(i, j) \in (\mathcal{C} \times \mathcal{C}) \backslash \mathcal{R}$ (we do not make any distinction in notation between the original function and its extension). Define the matrix $I_\kappa \in \mathbb{R}^{c \times c}$, called the *Laplacian* of $(\mathcal{C}, \mathcal{R}, \kappa)$, by

$$I_\kappa = \begin{bmatrix} \kappa_{11} - \sum_{i=1}^{c} \kappa_{1i} & \kappa_{21} & \cdots & \kappa_{c1} \\ \kappa_{12} & \kappa_{22} - \sum_{i=1}^{c} \kappa_{2i} & \cdots & \kappa_{c2} \\ \vdots & \vdots & \ddots & \vdots \\ \kappa_{1c} & \kappa_{2c} & \cdots & \kappa_{cc} - \sum_{i=1}^{c} \kappa_{ci} \end{bmatrix} \in \mathbb{R}^{c \times c}, \tag{2.8}$$

i.e.,

$$(I_\kappa)_{ij} = \begin{cases} \kappa_{ji}, & \text{if } i \neq j, \\ \kappa_{jj} - \sum_{i'=1}^{c} \kappa_{ji'}, & \text{if } i = j \end{cases} \qquad (i, j \in \overline{1, c}).$$

Note that both the rows and the columns of I_κ correspond to the vertices of the directed graph $(\mathcal{C}, \mathcal{R})$. (Other applications than CRNT may require to define the Laplacian as $-I_\kappa$, $I_\kappa^\top$, or $-I_\kappa^\top$.)

For the mass action system associated to the reaction network (2.5) we have $I_\kappa \in \mathbb{R}^{8 \times 8}$ and

$$I_\kappa = \left[\begin{array}{cc} \begin{matrix} -\kappa_{12} & \kappa_{21} & 0 & \kappa_{41} \\ \kappa_{12} & -(\kappa_{21} + \kappa_{23}) & 0 & 0 \\ 0 & \kappa_{23} & -\kappa_{34} & \kappa_{43} \\ 0 & 0 & \kappa_{34} & -(\kappa_{41} + \kappa_{43}) \end{matrix} & 0_{4 \times 4} \\ 0_{4 \times 4} & \begin{matrix} -\kappa_{56} & 0 & 0 & \kappa_{85} \\ \kappa_{56} & -\kappa_{67} & 0 & 0 \\ 0 & \kappa_{67} & -\kappa_{78} & 0 \\ 0 & 0 & \kappa_{78} & -\kappa_{85} \end{matrix} \end{array}\right], \tag{2.9}$$

where $0_{4 \times 4}$ is the 4×4 zero matrix.

Denote by $I \in \mathbb{R}^{c \times m}$ the *incidence matrix* of the directed graph $(\mathcal{C}, \mathcal{R})$, i.e., each row of I corresponds to a complex and each column of I corresponds to a reaction in such a way that the column corresponding to the reaction $(i, j) \in \mathcal{R}$ contains 1 in the jth row, -1 in the ith row, and 0 otherwise. Note that the column of I_κ that corresponds to the complex C_i is the linear combination of those columns of the incidence matrix I, which are corresponding to $\varrho^{\text{out}}(C_i)$, and the coefficients are given by the values of κ $(i \in \overline{1, c})$, where $\varrho^{\text{out}}(C_i)$ denotes the set of those reactions for which C_i is the reactant complex. More precisely, $(I_\kappa)_{\cdot i} = \sum_{a \in \varrho^{\text{out}}(C_i)} \kappa_a I_{\cdot a}$ for all $i \in \overline{1, c}$.

The incidence matrix of the directed graph $(\mathcal{C}, \mathcal{R})$ associated to the reaction network (2.5) is

$$I = \left[\begin{array}{cccccc|cccc} -1 & 1 & 0 & 0 & 0 & 1 & & & & \\ 1 & -1 & -1 & 0 & 0 & 0 & & \multicolumn{2}{c}{0_{4\times 4}} & \\ 0 & 0 & 1 & -1 & 1 & 0 & & & & \\ 0 & 0 & 0 & 1 & -1 & -1 & & & & \\ & & & & & & -1 & 0 & 0 & 1 \\ & & \multicolumn{2}{c}{0_{4\times 6}} & & & 1 & -1 & 0 & 0 \\ & & & & & & 0 & 1 & -1 & 0 \\ & & & & & & 0 & 0 & 1 & -1 \end{array}\right] \in \mathbb{R}^{8\times 10},$$

where $0_{4\times 4}$ and $0_{4\times 6}$ are the 4×4 and the 4×6 zero matrices, respectively.

Let us define the functions $\Theta : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^c_{\geq 0}$ and $R : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^m_{\geq 0}$ by

$$\Theta(x) = \begin{bmatrix} \prod_{s=1}^n x_s^{B_{s1}} \\ \prod_{s=1}^n x_s^{B_{s2}} \\ \vdots \\ \prod_{s=1}^n x_s^{B_{sc}} \end{bmatrix} \quad \text{and} \quad R(x) = \begin{bmatrix} \vdots \\ \kappa_{ij} \prod_{s=1}^n x_s^{B_{si}} \\ \vdots \end{bmatrix}_{(i,j)\in\mathcal{R}} \qquad (x \in \mathbb{R}^n_{\geq 0}),$$

respectively. Thus, Θ depends only on the reaction network, while R is also influenced by the rate coefficients. The coordinate function of R that corresponds to $(i, j) \in \mathcal{R}$ is called the *reaction rate function* of the reaction (i, j). Note that

$$I \cdot R(x) = I_\kappa \cdot \Theta(x) \text{ for all } x \in \mathbb{R}^n_{\geq 0}.$$

Let us define $f : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^n$ by

$$f(x) = \sum_{(i,j)\in\mathcal{R}} \kappa_{ij} \prod_{s=1}^n x_s^{B_{si}} \cdot (B_{\cdot j} - B_{\cdot i}) \text{ for } x \in \mathbb{R}^n_{\geq 0}. \tag{2.10}$$

With this, it is straightforward to see that

$$f(x) = B \cdot I_\kappa \cdot \Theta(x) = B \cdot I \cdot R(x) \text{ for all } x \in \mathbb{R}^n_{\geq 0},$$

which makes it possible to treat (2.6) in another equivalent forms. The one we will most often use is

$$\dot{x}(\tau) = B \cdot I_\kappa \cdot \Theta(x(\tau))$$

with state space $\mathbb{R}^n_{\geq 0}$. Thus, for the set of positive steady states E_+ (see (2.7)), we have

$$E_+ = \{x \in \mathbb{R}^n_+ \mid B \cdot I_\kappa \cdot \Theta(x) = 0\}.$$

The functions $\Theta : \mathbb{R}^5_{\geq 0} \to \mathbb{R}^8_{\geq 0}$ and $R : \mathbb{R}^5_{\geq 0} \to \mathbb{R}^{10}_{\geq 0}$ for the mass action system associated to

(2.5) are defined by

$$\Theta(x) = \begin{bmatrix} x_1x_2 \\ x_2^2 \\ x_4^2 \\ x_3x_4 \\ x_1x_5^3 \\ x_2 \\ x_4 \\ x_1x_3 \end{bmatrix} \quad \text{and} \quad R(x) = \begin{bmatrix} \kappa_{12}x_1x_2 \\ \kappa_{21}x_2^2 \\ \kappa_{23}x_2^2 \\ \kappa_{34}x_4^2 \\ \kappa_{43}x_3x_4 \\ \kappa_{41}x_3x_4 \\ \kappa_{56}x_1x_5^3 \\ \kappa_{67}x_2 \\ \kappa_{78}x_4 \\ \kappa_{85}x_1x_3 \end{bmatrix} \quad (x \in \mathbb{R}^5_{\geq 0}),$$

respectively.

2.4 The stoichiometric classes of chemical reaction networks

Recall from Sections 2.1 and 2.3 that $B \in \mathbb{R}^{n\times c}$ and $I \in \mathbb{R}^{c\times m}$ denote the matrix of complexes and the incidence matrix of the directed graph $(\mathcal{C}, \mathcal{R})$, respectively. The matrix $S = B\cdot I \in \mathbb{R}^{n\times m}$ is called the *stoichiometric matrix* of the reaction network. Note that, because of the structure of I, each column of S corresponds to a reaction (i, j) in such a way that the corresponding column is $B_{\cdot j} - B_{\cdot i} \in \mathbb{R}^n$, the net change of the species of the given reaction $((i, j) \in \mathcal{R})$. The range of S, $\operatorname{ran} S$, is called the *stoichiometric subspace*. For $q \in \mathbb{R}^n_{\geq 0}$, the set $(q + \operatorname{ran} S) \cap \mathbb{R}^n_{\geq 0}$ is called a *stoichiometric class*. A stoichiometric class $\mathcal{P}$ is called a *positive* one if $\mathcal{P} \cap \mathbb{R}^n_+ \neq \emptyset$ (we remark that this definition of a positive stoichiometric class is taken from [54, Section II], while it is not consistent with the one in [27, Subsection 5.2]). Clearly, (2.6) can be written as $\dot{x}(\tau) = S \cdot R(x(\tau))$, and thus the stoichiometric classes are forward invariant sets for (2.6). It is also apparent that the stoichiometric classes provide a partition of the nonnegative orthant $\mathbb{R}^n_{\geq 0}$. Therefore, the relevant way to look at the dynamics of a mass action system is to restrict it to a stoichiometric class.

For the reaction network (2.5) we have

$$S = \begin{bmatrix} -1 & 1 & 0 & 0 & 0 & 1 & -1 & 0 & 1 & 0 \\ 1 & -1 & -2 & 0 & 0 & 1 & 1 & -1 & 0 & 0 \\ 0 & 0 & 0 & 1 & -1 & -1 & 0 & 0 & 1 & -1 \\ 0 & 0 & 2 & -1 & 1 & -1 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -3 & 0 & 0 & 3 \end{bmatrix} \in \mathbb{R}^{5\times 10}.$$

One can easily see that the range of S, $\operatorname{ran} S$, equals to $\mathbb{R}^5$. For such examples, where $\operatorname{ran} S$ is strictly smaller than $\mathbb{R}^n$, see e.g. the reaction network (3.6) in Chapter 3.

2.5 The linkage classes of chemical reaction networks

To continue the exposition of the notions related to chemical reaction networks, we need some standard notions from the theory of directed graphs (e.g. weak component and strong connectedness of directed graphs). General references on graph theory are e.g. [9] and [51]. We have also collected the required notions from graph theory in Appendix A.

Denote by ℓ the number of weak components of the directed graph $(\mathcal{C},\mathcal{R})$ and by

$$(\mathcal{C}^1,\mathcal{R}^1),(\mathcal{C}^2,\mathcal{R}^2),\ldots,(\mathcal{C}^\ell,\mathcal{R}^\ell)$$

the weak components themselves. Let $c^r=|\mathcal{C}^r|$ $(r\in\overline{1,\ell})$. As a consequence of the assumptions on $\mathcal{R}$ (see Section 2.1), we have $c^r\geq 2$ for all $r\in\overline{1,\ell}$. The weak components of $(\mathcal{C},\mathcal{R})$ are called *linkage classes* in CRNT. In case all the linkage classes of $(\mathcal{C},\mathcal{R})$ are strongly connected, the network is called *weakly reversible* in CRNT.

The strong components of $(\mathcal{C},\mathcal{R})$ are called *strong linkage classes* in CRNT. Denote by t the number of absorbing strong components of $(\mathcal{C},\mathcal{R})$. The absorbing strong components of $(\mathcal{C},\mathcal{R})$ are called *terminal strong linkage classes* in CRNT. Since each weak component of a directed graph contains at least one absorbing strong component, the inequality $\ell\leq t$ obviously holds. We will assume in most of the results presented in this thesis that the reaction network under consideration satisfies $\ell=t$. Moreover, in certain situations we will assume weak reversibility. It is explained in [27, Appendix IV] why mass action models derived from reaction networks with $\ell<t$ possess some kind of degeneracy.

For the reaction network (2.5) we have two linkage classes (i.e., $\ell=2$). The linkage classes are denoted by $(\mathcal{C}^1,\mathcal{R}^1)$ and $(\mathcal{C}^2,\mathcal{R}^2)$, where

$$\begin{aligned}
&\mathcal{C}^1=\{C_1,C_2,C_3,C_4\},\mathcal{R}^1=\{(1,2),(2,1),(2,3),(3,4),(4,3),(4,1)\},\\
&\mathcal{C}^2=\{C_5,C_6,C_7,C_8\},\text{ and }\mathcal{R}^2=\{(5,6),(6,7),(7,8),(8,5)\}.
\end{aligned}$$

Also, we have $c^1=4$ and $c^2=4$. Since both $(\mathcal{C}^1,\mathcal{R}^1)$ and $(\mathcal{C}^2,\mathcal{R}^2)$ are strongly connected, the network (2.5) is weakly reversible (and consequently, $\ell=t$ holds).

For an example, where $\ell<t$, see the reaction network

$$2X_1 \longleftarrow X_1+X_2 \longrightarrow 2X_2.$$

2.6 Some basic properties of the incidence matrix and the Laplacian

In this section, we have collected some standard results concerning the kernel, the range, and the rank of the matrices I and I_κ (recall the definitions of I and I_κ from Section 2.3). Especially the matrix I_κ plays an important role in the qualitative properties of mass action systems (recall from Section 2.3 that the ODE to be examined is $\dot{x}(\tau)=B\cdot I_\kappa\cdot\Theta(x(\tau))$).

As we already mentioned in Section 2.3, each column of I_κ is a linear combination of certain columns of I. As a consequence, we directly obtain that $\operatorname{ran} I_\kappa$ is a linear subspace $\operatorname{ran} I$. We will see in this section that if $\ell = t$ (i.e., each linkage class contains only one terminal strong linkage class) then these two linear subspaces of $\mathbb{R}^c$ coincide. In particular, if $\ell = t$ then $\operatorname{ran} I_\kappa$ does not depend on the values of κ.

It will be useful in the sequel to have in hand the concept of the excess function on directed graphs. Please refer to Appendix A for the definition of this standard graph theoretical notion. The following proposition is a direct consequence of the definitions of the matrix I_κ and the excess function.

Proposition 2.3 *Let (V, A, κ) be a labelled directed graph with $\kappa : A \to \mathbb{R}$ (i.e., κ can take any real value) and let I_κ be as in* (2.8)*. Let $y : V \to \mathbb{R}$ be any function and define $z : A \to \mathbb{R}$ by $z_{(i,j)} = \kappa_{ij} y_i$ $((i,j) \in A)$. Then*

$$\operatorname{excess}_z(U) = \sum_{j \in U} (I_\kappa y)_j \textit{ for all } U \subseteq V.$$

Proof Fix $j \in V$. Then, by the definitions of the matrix I_κ and the excess function we obtain

$$(I_\kappa y)_j = \sum_{i \in V} (I_\kappa)_{ji} y_i = \sum_{i \in V \setminus \{j\}} \kappa_{ij} y_i - \sum_{i \in V \setminus \{j\}} \kappa_{ji} y_j = z(\varrho^{\text{in}}(j)) - z(\varrho^{\text{out}}(j)) = \operatorname{excess}_z(j),$$

where $\varrho^{\text{in}}(j)$ and $\varrho^{\text{out}}(j)$ denote the sets of arcs that enter j and leave j, respectively, and the notations $z(\varrho^{\text{in}}(j))$ and $z(\varrho^{\text{out}}(j))$ are understood in accordance with (1.1). The statement of the proposition then follows from the additivity of the excess function (see (A.1) in Appendix A). $\square$

Remark 2.4 Let us now give further explanation on the objects occurring in Proposition 2.3. Let (V, A) be a directed graph for which $\varrho^{\text{out}}(i) \neq \emptyset$ for all $i \in V$. Let $\kappa : V \times V \to \mathbb{R}_{\geq 0}$ be a function for which $\kappa_{ij} > 0$ if and only if $(i,j) \in A$ and let $h : V \to \mathbb{R}$ be a function for which $\sum_{i \in V} h_i = 0$. We will define two sets of functions, which we denote by $Z_{\kappa,h}$ and $Y_{\kappa,h}$, respectively, and we will point out that there is a one-to-one correspondence between them.

Denote by $Z_{\kappa,h}$ the set of functions $z : A \to \mathbb{R}$ for which

$$\frac{z_{a_1}}{\kappa_{a_1}} = \frac{z_{a_2}}{\kappa_{a_2}} \text{ for all } i \in V \text{ and for all } a_1, a_2 \in \varrho^{\text{out}}(i) \text{ and} \tag{2.11}$$

$$\operatorname{excess}_z(i) = h_i \text{ for all } i \in V \tag{2.12}$$

hold. In words, condition (2.11) means that if a_1 and a_2 are two arcs with the same tail then the fraction z_{a_1}/κ_{a_1} equals to the fraction z_{a_2}/κ_{a_2}. The fact that makes functions satisfying (2.11) important in the context of CRNT is that if two reactions, say a_1 and a_2, have the same reactant complex then the rate functions R_{a_1} and R_{a_2} satisfy $\frac{R_{a_1}(x)}{\kappa_{a_1}} = \frac{R_{a_2}(x)}{\kappa_{a_2}}$ for all concentrations $x \in \mathbb{R}^n_{\geq 0}$. Condition (2.12) expresses that the function excess_z equals to some given function h. (If (2.12) holds for a function $z : A \to \mathbb{R}$ then z is called an *h-transshipment* in the literature of graph theory [51].)

Denote by $Y_{\kappa,h}$ the set of functions $y : V \to \mathbb{R}$ for which $I_\kappa y = h$. Let us define $w : Y_{\kappa,h} \to Z_{\kappa,h}$ in the following way. For $y \in Y_{\kappa,h}$ define $w(y) = z : A \to \mathbb{R}$ by $z_{(i,j)} = \kappa_{ij} y_i$ $((i,j) \in A)$. It is left to the reader to check that $w(y)$ is indeed an element of $Z_{\kappa,h}$ and that $w : Y_{\kappa,h} \to Z_{\kappa,h}$ is a bijection. It is also straightforward to see that $Y_{\kappa,h} \neq \emptyset$ if and only if $Z_{\kappa,h} \neq \emptyset$. As a conclusion, we intended to show the correspondence between certain objects of graph theoretical nature and of linear algebraic nature.

Note that if there exists an $i \in V$ such that $\varrho^{\text{out}}(i) = \emptyset$ then w is not injective. Moreover, if we consider $Y_{\kappa,h}$ and $Z_{\kappa,h}$ as affine subspaces of $\mathbb{R}^{|V|}$ and $\mathbb{R}^{|A|}$, respectively, then $\dim Y_{\kappa,h} - \dim Z_{\kappa,h} = |\{i \in V \mid \varrho^{\text{out}}(i) = \emptyset\}|$ (provided that $Y_{\kappa,h} \neq \emptyset$). As a matter of fact, Lemma 2.5 below tells us that $\dim Y_{\kappa,h}$ equals to the number of absorbing strong components of (V, A). $\square$

For a vector $y \in \mathbb{R}^c$, denote by $\operatorname{supp}(y)$ the *support* of y, i.e., $\operatorname{supp}(y) = \{i \in \overline{1,c} \mid y_i \neq 0\}$. The following lemma describes the kernel of I_κ.

Lemma 2.5 *Let (V, A, κ) be a labelled directed graph with $\kappa : A \to \mathbb{R}_+$ (i.e., κ can take only positive values) and let I_κ be as in (2.8). Denote by t the number of absorbing strong components of (V, A) and denote the vertex sets of these components by $V^1, V^2, \ldots, V^t$. Let $V'' = V \setminus (\cup_{k=1}^t V^k)$. Denote by I''_κ the $|V''| \times |V''|$ submatrix of I_κ with rows and columns corresponding to V''. Then I''_κ is invertible (provided that $V'' \neq \emptyset$), $\dim \ker I_\kappa = t$, and there exists a basis $y^1, y^2, \ldots, y^t \in \mathbb{R}^{|V|}_{\geq 0}$ in $\ker I_\kappa$ such that $\operatorname{supp}(y^k) = V^k$ for all $k \in \overline{1,t}$.*

Proof Denote by I^k_κ the $|V^k| \times |V^k|$ submatrix of I_κ with rows and columns corresponding to V^k $(k \in \overline{1,t})$. Since $\varrho^{\text{out}}(V^k) = \emptyset$ for all $k \in \overline{1,t}$, the matrix I_κ can be considered in the block form

$$I_\kappa = \begin{bmatrix} I^1_\kappa & 0 & \cdots & 0 & * \\ 0 & I^2_\kappa & \cdots & 0 & * \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & I^t_\kappa & * \\ 0 & 0 & \cdots & 0 & I''_\kappa \end{bmatrix} \in \mathbb{R}^{\left(\sum_{k=1}^t |V^k| + |V''|\right) \times \left(\sum_{k=1}^t |V^k| + |V''|\right)}. \tag{2.13}$$

First, we show that I''_κ is invertible if $V'' \neq \emptyset$. To this end, let $y'' \in \mathbb{R}^{|V''|}$ be any vector in $\ker I''_\kappa$ and let $y \in \mathbb{R}^{|V|}$ be any extension of y'' (i.e., $y_i = y''_i$ for all $i \in V''$). Let us partition V'' into 3 sets in the following way. Let

$$\begin{aligned} V''_- &= \{i \in V'' \mid y''_i < 0\}, \\ V''_0 &= \{i \in V'' \mid y''_i = 0\}, \text{ and} \\ V''_+ &= \{i \in V'' \mid y''_i > 0\}. \end{aligned}$$

Then clearly V'' is the disjoint union of V''_-, V''_0, and V''_+. Once we show that $V''_- = V''_+ = \emptyset$, the invertibility of I''_κ follows. Let us define $z : A \to \mathbb{R}$ as in Proposition 2.3, i.e., $z_{(i,j)} = \kappa_{ij} y_i$ for $(i, j) \in A$. Since $I''_\kappa y'' = 0$, we have

$$\operatorname{excess}_z(V''_-) = \sum_{j \in V''_-} (I_\kappa y)_j \overset{(2.13)}{=} \sum_{j \in V''_-} (I''_\kappa y'')_j = 0.$$

Note that $z_a < 0$ for all $a \in \varrho^{\text{out}}(V''_-)$ and $z_a \geq 0$ for all $a \in \varrho^{\text{in}}(V''_-)$. Hence, the set $\varrho^{\text{out}}(V''_-)$ must be empty (otherwise $\text{excess}_z(V''_-)$ would be positive). However, if $V''_- \neq \emptyset$ then, by the finiteness of V, V''_- must contain an absorbing strong component, which contradicts the definition of V''. Hence $V''_- = \emptyset$. Similar reasoning shows that $V''_+ = \emptyset$. So we have shown that the kernel of I''_κ is trivial, and hence, I''_κ is invertible.

Since $\ker I''_\kappa$ is trivial, it is clear from (2.13) that it suffices to examine $\ker I^1_\kappa, \ker I^2_\kappa, \dots, \ker I^t_\kappa$ separately for a description of $\ker I_\kappa$. Fix $k \in \overline{1,t}$ and let $y \in \mathbb{R}^{|V^k|}$ be an element of $\ker I^k_\kappa$. We claim that

$$\text{sgn}(y_i) = \text{sgn}(y_j) \text{ for all } i, j \in V^k. \tag{2.14}$$

To prove this claim, we partition V^k into 3 sets in the following way. Let

$$\begin{aligned} V^k_- &= \{i \in V^k \mid y_i < 0\}, \\ V^k_0 &= \{i \in V^k \mid y_i = 0\}, \text{ and} \\ V^k_+ &= \{i \in V^k \mid y_i > 0\}. \end{aligned}$$

Similar reasoning as in the proof of the invertibility of I''_κ shows that $\varrho^{\text{out}}(V^k_-) = \emptyset$ and $\varrho^{\text{out}}(V^k_+) = \emptyset$. Since each strong component is strongly connected, this implies that either $V^k_- = V^k$ or $V^k_+ = V^k$ or $V^k_0 = V^k$. Hence, (2.14) indeed holds.

Since the sum of the rows of the square matrix I^k_κ is the zero vector, $\ker I^k_\kappa$ is nontrivial. Since (2.14) holds, $\ker I^k_\kappa$ must be contained in $\mathbb{R}^{|V^k|}_+ \cup \mathbb{R}^{|V^k|}_- \cup \{0\}$. Since $\mathbb{R}^{|V^k|}_+ \cup \mathbb{R}^{|V^k|}_- \cup \{0\}$ cannot contain a two-dimensional linear space, we have $\dim \ker I^k_\kappa = 1$.

As a consequence, taking also into account (2.13) and (2.14),

there exists a basis $y^1, y^2, \dots, y^t \in \mathbb{R}^{|V|}_{\geq 0}$ in $\ker I_\kappa$ such that $\text{supp}(y^k) = V^k$ for all $k \in \overline{1,t}$.

□

We remark that another proof of Lemma 2.5 is provided in [32, Appendix]. We summarise the main steps of that proof here (but with our notation and terminology). Let $y \in \ker I_\kappa$. The authors first show that the vector, which is obtained by taking the absolute value of the coordinates of y is also in $\ker I_\kappa$. The next step is to show that if $i, j \in V$ are such that $y_j = 0$ and there exists a directed walk from i to j then $y_i = 0$. After this, they show that $\text{supp}(y) \subset \cup_{k=1}^t V^k$. Then they prove that for all $k \in \overline{1,t}$ the equality $\dim \ker I^k_\kappa = 1$ holds and $\ker I^k_\kappa$ can be generated by a vector, all of which coordinates are positive. After this, the conclusion of the lemma follows easily.

We also remark that a special case of Lemma 2.5 is proven also in [54, Section V]. That proof makes use of the Perron-Frobenius Theorem.

Remark 2.6 As a side remark, we mention here that Lemma 2.5 allows us to describe the stationary distributions of a discrete-time homogeneous Markov chain with finite state space. Denote by S the state space and by $P \in \mathbb{R}^{|S| \times |S|}$ the transition matrix of the chain. Then, by definition, $y \in \mathbb{R}^{|S|}$ is a stationary distribution of the chain if y is a probability distribution on S and $y^\top = y^\top P$, or equivalently, $y \in \ker(P^\top - \mathrm{Id})$, where $\mathrm{Id} \in \mathbb{R}^{|S|\times|S|}$ is the $|S| \times |S|$ identity matrix. Lemma 2.5 implies that if the essential classes of the chain are $S^1, S^2, \dots, S^t$ then there exist probability distributions $y^1, y^2, \dots, y^t$ on S such that for all $k \in \overline{1,t}$ and for all $i \in S$, $y_i^k > 0$ if and only if $i \in S^k$. It also holds that all the stationary distributions of the chain can be obtained by taking all the convex combinations of $y^1, y^2, \dots, y^t$. □

Our next aim is to provide a description of the range of the incidence matrix of the directed graph $(\mathcal{C}, \mathcal{R})$. Recall that the linkage classes of $(\mathcal{C}, \mathcal{R})$ are denoted by $(\mathcal{C}^1, \mathcal{R}^1), \dots, (\mathcal{C}^\ell, \mathcal{R}^\ell)$. Let

$$e^1, e^2, \dots, e^\ell \in \{0,1\}^c$$

be the characteristic vectors of the sets $\mathcal{C}^1, \mathcal{C}^2, \dots, \mathcal{C}^\ell$, respectively, i.e., for all $r \in \overline{1,\ell}$ and for all $i \in \mathcal{C}$ we have

$$\begin{aligned} e_i^r &= 1 \text{ if } i \in \mathcal{C}^r \text{ and} \\ e_i^r &= 0 \text{ if } i \in \mathcal{C} \backslash \mathcal{C}^r. \end{aligned}$$

One can easily prove Proposition 2.7 below. For a way to prove it, please refer to [10, Section 4.2]. The sketch of that proof can also be found in [12, Appendix A.2].

Proposition 2.7 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Denote by I the incidence matrix of the directed graph $(\mathcal{C}, \mathcal{R})$, by c the number of complexes (i.e., $c = |\mathcal{C}|$), and by ℓ the number of linkage classes. Then* $\operatorname{rank} I = c - \ell$ *and* $\operatorname{ran} I = (\operatorname{span}(e^1, e^2, \dots, e^\ell))^\perp$.

For further convenience, let

$$L = [e^1, e^2, \dots, e^\ell]. \tag{2.15}$$

Thus, L is a $c \times \ell$ matrix. By Proposition 2.7, we have $\operatorname{ran} I = (\operatorname{ran} L)^\perp$, or equivalently, $\operatorname{ran} I = \ker L^\top$. As we mentioned earlier, $\operatorname{ran} I_\kappa$ is a linear subspace of $\operatorname{ran} I$ (regardless of the values of the rate coefficients). The next corollary tells us that if each linkage class contains only one terminal strong linkage class then $\operatorname{ran} I_\kappa$ equals to $\operatorname{ran} I$.

Corollary 2.8 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system. Denote by ℓ and t the number of linkage classes and the number of terminal strong linkage classes, respectively. Assume that $\ell = t$. Then* $\operatorname{ran} I = \operatorname{ran} I_\kappa$.

Proof By Proposition 2.7, $\operatorname{rank} I = c - \ell$. By Lemma 2.5 and Proposition B.3, $\operatorname{rank} I_\kappa = c - t$. Thus, if $\ell = t$ then $\operatorname{rank} I = \operatorname{rank} I_\kappa$. Since $\operatorname{ran} I_\kappa$ is a linear subspace of $\operatorname{ran} I$, we have $\operatorname{ran} I = \operatorname{ran} I_\kappa$. □

Recall that in case of the reaction network (2.5), the matrix I_κ takes the form (2.9) for the associated mass action system. A short calculation shows that the $y^1, y^2 \in \mathbb{R}^8$ guaranteed to exist by Lemma 2.5 for (2.9) can be chosen as

$$y^1 = \begin{bmatrix} (\kappa_{21}+\kappa_{23})\kappa_{34}\kappa_{41} \\ \kappa_{12}\kappa_{34}\kappa_{41} \\ \kappa_{12}\kappa_{23}(\kappa_{41}+\kappa_{43}) \\ \kappa_{12}\kappa_{23}\kappa_{34} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad \text{and} \quad y^2 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \kappa_{67}\kappa_{78}\kappa_{85} \\ \kappa_{56}\kappa_{78}\kappa_{85} \\ \kappa_{56}\kappa_{67}\kappa_{85} \\ \kappa_{56}\kappa_{67}\kappa_{78} \end{bmatrix},$$

respectively. Note also that for the reaction network (2.5) we have

$$e^1 = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \in \{0,1\}^8, \quad e^2 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} \in \{0,1\}^8, \quad \text{and} \quad L = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{bmatrix} \in \{0,1\}^{8\times 2}.$$

Finally, by Proposition 2.7 and Corollary 2.8, we have

$$\operatorname{ran} I = \operatorname{ran} I_\kappa = \{v \in \mathbb{R}^8 \mid v_1 + v_2 + v_3 + v_4 = 0 \text{ and } v_5 + v_6 + v_7 + v_8 = 0\}.$$

2.7 The deficiency of chemical reaction networks

An integer number, called the deficiency, can be associated to each reaction network $(\mathcal{X},\mathcal{C},\mathcal{R})$. In Chapters 3, 4, 5, and 6 we will prove statements about the set of positive steady states of mass action systems. We will usually carry out these under some assumptions on the deficiency of the underlying reaction network. Recall the definitions of n, c, m, B, I, I_κ, S, and ℓ from Sections 2.1, 2.3, 2.4, and 2.5. The following definition of the deficiency is due to Horn [38] and Feinberg [27].

Definition 2.9 *For a reaction network* $(\mathcal{X},\mathcal{C},\mathcal{R})$ *define the* deficiency *by* $\delta = c - \ell - \operatorname{rank} S$.

In words, the deficiency is the number of complexes minus the number of linkage classes minus the dimension of the stoichiometric subspace. For the reaction network (2.5) we have $\delta = 8-2-5 = 1$. We emphasise that the deficiency is associated to a reaction network and does not depend on the rate coefficients associated to the reaction network. Thus, when we speak of the deficiency of a mass action system, we mean the deficiency of the underlying reaction network. The following proposition makes it possible to define the deficiency in another equivalent ways. It is apparent from the following proposition that the deficiency is a nonnegative integer (this fact is not so obvious at first glance from Definition 2.9).

Proposition 2.10 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Let B, I, S, and δ be the matrix of complexes, the incidence matrix of $(\mathcal{C}, \mathcal{R})$, the stoichiometric matrix, and the deficiency, respectively. Then*

$$\delta = \dim\ker S - \dim\ker I = \dim(\ker B \cap \operatorname{ran} I).$$

Proof Propositions B.3 and 2.7 imply that

$$\dim\ker S - \dim\ker I = (m - \operatorname{rank} S) - (m - \operatorname{rank} I) = c - \ell - \operatorname{rank} S = \delta.$$

The equality $\dim\ker S - \dim\ker I = \dim(\ker B \cap \operatorname{ran} I)$ follows from the fact that $S = B \cdot I$ (see Proposition B.4). $\square$

Since $S = B \cdot I$, the linear space $\ker I$ is a linear subspace of $\ker S$. By Proposition 2.10, the deficiency measures the difference between the dimensions of these two linear spaces.

Proposition 2.7 and the fact that $\delta = \dim(\ker B \cap \operatorname{ran} I)$ allow us to introduce a matrix whose kernel's dimension is the deficiency. Define the block matrix $\widehat{B} \in \mathbb{R}^{(n+\ell)\times c}$ by

$$\widehat{B} = \begin{bmatrix} B \\ L^\top \end{bmatrix} \in \mathbb{R}^{(n+\ell)\times c}, \tag{2.16}$$

where B is the matrix of complexes and L is as in (2.15). In words, the $(n+r)$th row of $\widehat{B}$ is $(e^r)^\top$ $(r \in \overline{1,\ell})$, where $e^1, e^2, \ldots, e^\ell$ are as in Section 2.6. We call $\widehat{B}$ the *augmented matrix of complexes*.

Proposition 2.11 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Let $\widehat{B}$ and δ be the augmented matrix of complexes and the deficiency, respectively. Then $\ker \widehat{B} = \ker B \cap \operatorname{ran} I$ and $\delta = \dim\ker \widehat{B}$.*

Proof Since $\ker L^\top = \operatorname{ran} I$ (see Section 2.6), we have $\ker \widehat{B} = \ker B \cap \operatorname{ran} I$. The equality $\delta = \dim\ker \widehat{B}$ follows from Proposition 2.10. $\square$

We remark that the equality $\delta = \dim\ker \widehat{B}$ appears implicitly in [38] and [26] and explicitly in [17]. It will turn out that it is useful to think of the deficiency of a reaction network as the dimension of $\ker \widehat{B}$. We will see in Chapters 3, 4, and 5 that the matrix $\widehat{B}$ shows up naturally when investigating the set of positive steady states of a mass action system. We remark that the nonnegativity of the deficiency is also apparent from the fact that $\delta = \dim\ker \widehat{B}$. Further consequence is that the deficiency is not dependent on how reactions connect complexes inside linkage classes. In other words, once it is specified which complexes correspond to which linkage classes, the deficiency is determined.

The following description of the deficiency is especially important from the point of view of the proofs in Chapters 4 and 5.

Proposition 2.12 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system. Denote by ℓ and t the number of linkage classes and the number of terminal strong linkage classes, respectively. Let B, I_κ, and δ be the matrix of complexes, the Laplacian of $(\mathcal{C}, \mathcal{R}, \kappa)$, and the deficiency, respectively. Assume that $\ell = t$. Then $\ker \widehat{B} = \ker B \cap \operatorname{ran} I_\kappa$ and $\delta = \dim(\ker B \cap \operatorname{ran} I_\kappa)$.*

Proof The statement directly follows from Corollary 2.8 and Proposition 2.11. $\square$

Clearly, one can define the deficiency not only for the whole network, but also for each linkage class. Let $m^r = |\mathcal{R}^r|$ $(r \in \overline{1,\ell})$. Consider the matrix S in the block form

$$S = [S^1, S^2, \ldots, S^\ell],$$

where $S^r \in \mathbb{R}^{n \times m^r}$ and the columns of S^r correspond to the reactions in $\mathcal{R}^r$ $(r \in \overline{1,\ell})$.

Definition 2.13 *For a reaction network* $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *define the* deficiency of the rth linkage class *by* $\delta^r = c^r - 1 - \operatorname{rank} S^r$ $(r \in \overline{1,\ell})$.

Consider also $\widehat{B}$ in the block form

$$\widehat{B} = [\widehat{B}^1, \widehat{B}^2, \ldots, \widehat{B}^\ell],$$

where $\widehat{B}^r \in \mathbb{R}^{(n+\ell) \times c^r}$ and the columns of $\widehat{B}^r$ are corresponding to the complexes in $\mathcal{C}^r$ $(r \in \overline{1,\ell})$. As a consequence of Proposition 2.11, we obtain the following proposition.

Proposition 2.14 *Let* $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *be a reaction network with* ℓ *linkage classes and fix* $r \in \overline{1,\ell}$. *Let* $\widehat{B}^r$ *be as above and let* δ^r *be the deficiency of the* r*th linkage class. Then* $\delta^r = \dim \ker \widehat{B}^r$.

The following proposition shows that the sum of the deficiencies of the linkage classes cannot exceed the deficiency of the whole network, i.e.,

$$\delta \geq \delta^1 + \delta^2 + \cdots + \delta^\ell.$$

Clearly, a mass action system with ℓ linkage classes can be decomposed in a natural way into ℓ mass action systems. In Chapter 3 we will examine the relation between the set of positive steady states of these ℓ mass action systems and the set of positive steady states of the original mass action system under the assumption $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$. It is useful to formulate the condition $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$ in terms of the matrices S and $\widehat{B}$.

Proposition 2.15 *Let* $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *be a reaction network with* ℓ *linkage classes. Let* S, $\widehat{B}$, *and* δ *be the stoichiometric matrix, the augmented matrix of complexes, and the deficiency, respectively. Also, let* $S^1, S^2, \ldots, S^\ell$, $\widehat{B}^1, \widehat{B}^2, \ldots, \widehat{B}^\ell$, *and* $\delta^1, \delta^2, \ldots, \delta^\ell$ *be as above. Then*

$$\delta \geq \delta^1 + \delta^2 + \cdots + \delta^\ell. \tag{2.17}$$

Moreover, the following are equivalent.

(A) $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$,

(B) $\operatorname{ran} S = \operatorname{ran} S^1 \oplus \operatorname{ran} S^2 \oplus \cdots \oplus \operatorname{ran} S^\ell$, *and*

(C) $\operatorname{ran} \widehat{B} = \operatorname{ran} \widehat{B}^1 \oplus \operatorname{ran} \widehat{B}^2 \oplus \cdots \oplus \operatorname{ran} \widehat{B}^\ell$.

Proof Note that $\operatorname{rank}\widehat{B} \leq \sum_{r=1}^{\ell} \operatorname{rank}\widehat{B}^r$, where equality holds if and only if $\operatorname{ran}\widehat{B} = \oplus_{r=1}^{\ell} \operatorname{ran}\widehat{B}^r$. Hence,

$$\sum_{r=1}^{\ell} \delta^r = \sum_{r=1}^{\ell} \dim\ker\widehat{B}^r = \sum_{r=1}^{\ell}(c^r - \operatorname{rank}\widehat{B}^r) = c - \sum_{r=1}^{\ell} \operatorname{rank}\widehat{B}^r \leq c - \operatorname{rank}\widehat{B} = \dim\ker\widehat{B} = \delta.$$

Thus, we have obtained (2.17) and also the equivalence of (A) and (C).

Similarly, $\operatorname{rank} S \leq \sum_{r=1}^{\ell} \operatorname{rank} S^r$, where equality holds if and only if $\operatorname{ran} S = \oplus_{r=1}^{\ell} \operatorname{ran} S^r$. Hence,

$$\sum_{r=1}^{\ell} \delta^r = \sum_{r=1}^{\ell}(c^r - 1 - \operatorname{rank} S^r) = c - \ell - \sum_{r=1}^{\ell} \operatorname{rank} S^r \leq c - \ell - \operatorname{rank} S = \delta,$$

which shows (the inequality (2.17) and) the equivalence of (A) and (B). □

For the reaction network (2.5) we have

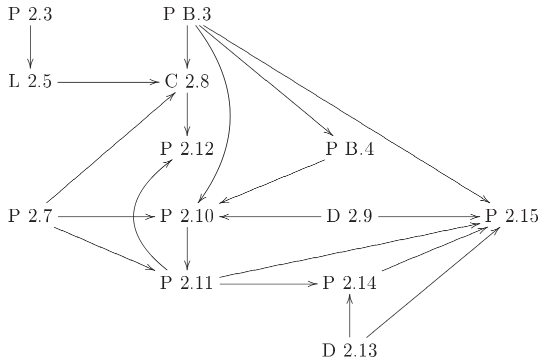
$$\widehat{B} = \begin{bmatrix} 1 & 0 & 0 & 0 & 1 & 0 & 0 & 1 \\ 1 & 2 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 2 & 1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 3 & 0 & 0 & 0 \\ 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{bmatrix} \in \mathbb{R}^{(5+2)\times 8} \quad \text{and} \quad \ker\widehat{B} = \operatorname{span}\left(\begin{bmatrix} 0 \\ -1 \\ 1 \\ 0 \\ 0 \\ 2 \\ -2 \\ 0 \end{bmatrix}\right).$$

A short calculation shows that for the reaction network (2.5) we have $\delta^1 = 4 - 1 - 3 = 0$ and $\delta^2 = 4 - 1 - 3 = 0$, thus $\delta > \delta^1 + \delta^2$ (recall from the beginning of this section that $\delta = 8 - 2 - 5 = 1$ for (2.5)).

2.8 The acyclic directed graph of the implications

We have depicted below the acyclic directed graph of the implications of this chapter. The vertex set consists of definitions (D), propositions (P), lemmas (L), theorems (T), and corollaries (C). All the proven propositions, lemmas, theorems, and corollaries of this chapter are in the vertex set (e.g. P 2.3, L 2.5, and C 2.8 are vertices). In addition, those definitions and statements (possibly from other chapters) are also in the vertex set, which are used in the proofs of this chapter (e.g. D 2.9 and P B.3 are also vertices). The ordered pair (i, j) of such vertices is an arc of the directed graph if i is used in the course of the proof of j (e.g. (P 2.7, P 2.10) and (D 2.9, P 2.15) are in the arc set).

A similarly built acyclic directed graph is also drawn at the ends of Chapters 3, 4, 5, and 6, respectively.



2.9 Summary of the notations

We summarise in Tables 2.1 and 2.2 those notations concerning reaction networks and mass action systems, respectively, that are used throughout this thesis. Thus, Tables 2.1 and 2.2 also separate those notions that are related purely to reaction networks (i.e., those that are independent of the dynamics associated to the reaction network) from those notions that are related to the dynamics. E.g. the deficiency is a notion associated to a reaction network, it does not depend on the dynamics assigned to the reaction network in question, and therefore the deficiency is recorded in Table 2.1. Since e.g. the set of positive steady states does depend on the dynamics assigned to the reaction network in question, it is recorded in Table 2.2.

Though the deficiency, the linkage classes, etc. are notions related to reaction networks, we often speak about the deficiency, the linkage classes, etc. of a mass action system. Naturally, these are understood as the deficiency, the linkage classes, etc. of the underlying reaction network of the mass action system in question.

Our intention throughout this thesis is to treat notations in a unified manner. Thus, unless stated otherwise, the notations $(\mathcal{C}, \mathcal{R})$, B, ℓ, etc. mean the graph of complexes, the matrix of complexes, the number of linkage classes, etc. throughout this thesis. We also try for a unified usage of running indices. Thus, elements of $\overline{1, c}$ are usually denoted by the symbols i, j, i_1, i_2, i', i'', etc. Accordingly, elements of $\mathcal{R}$ are usually denoted by (i, j), (i_1, i_2), (j_1, j_2), (i, i'), etc. An element of $\overline{1, n}$ is usually denoted by s, while an element of $\overline{1, \ell}$ is usually denoted by r.

n	the number of species
$\mathcal{X} = \{X_1, X_2, \ldots, X_n\}$	the set of species
c	the number of complexes
$\mathcal{C} = \{C_1, C_2, \ldots, C_c\}$	the set of complexes
m	the number of reactions
$\mathcal{R}$	the set of reactions
$(\mathcal{X}, \mathcal{C}, \mathcal{R})$	reaction network
$B \in \mathbb{R}^{n \times c}$	the matrix of complexes
$(\mathcal{C}, \mathcal{R})$	the graph of complexes
ℓ	the number of linkage classes
$(\mathcal{C}^1, \mathcal{R}^1), (\mathcal{C}^2, \mathcal{R}^2), \ldots, (\mathcal{C}^\ell, \mathcal{R}^\ell)$	the linkage classes
$c^1, c^2, \ldots, c^\ell$	the number of complexes in the linkage classes
$m^1, m^2, \ldots, m^\ell$	the number of reactions in the linkage classes
t	the number of terminal strong linkage classes
$I \in \mathbb{R}^{c \times m}$	the incidence matrix of $(\mathcal{C}, \mathcal{R})$
$e^1, e^2, \ldots, e^\ell$	a basis in $(\operatorname{ran} I)^\perp$
$L = [e^1, e^2, \ldots, e^\ell] \in \mathbb{R}^{c \times \ell}$	$\operatorname{ran} I = (\operatorname{ran} L)^\perp = \ker L^\top$
$\widehat{B} = \begin{bmatrix} B \\ L^\top \end{bmatrix} \in \mathbb{R}^{(n+\ell) \times c}$	the augmented matrix of complexes
$\mathbb{R}^{n \times m} \ni S = B \cdot I =$ $= [\cdots, B_{\cdot j} - B_{\cdot i}, \cdots]_{(i,j) \in \mathcal{R}}$	the stoichiometric matrix
$\mathcal{S} = \operatorname{ran} S$	the stoichiometric subspace (in $\mathbb{R}^n$)
$\delta = c - \ell - \operatorname{rank} S =$ $= \dim \ker S - \dim \ker I =$ $= \dim(\ker B \cap \operatorname{ran} I) =$ $= \dim \ker \widehat{B}$	the deficiency
$\delta^1, \delta^2, \ldots, \delta^\ell$	the deficiencies of the linkage classes

Table 2.1: Summary of the notations related to reaction networks.

$\kappa : \mathcal{R} \to \mathbb{R}_+$	the rate coefficient function
$(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$	mass action system
$I_\kappa \in \mathbb{R}^{c \times c}$	the Laplacian matrix of the labelled directed graph $(\mathcal{C}, \mathcal{R}, \kappa)$
$x(\tau) = [x_1(\tau), x_2(\tau), \ldots, x_n(\tau)]^\top$	the concentration of the species at time τ
$\Theta_i(x) = \prod_{s=1}^n x_s^{B_{si}}$	the monomial associated to $C_i = B_{1i}X_1 + \cdots + B_{ni}X_n$
$\Theta = [\Theta_1, \Theta_2, \ldots, \Theta_c]^\top : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^c_{\geq 0}$	the monomial functions associated to the complexes
$R_{(i,j)}(x) = \kappa_{ij} \prod_{s=1}^n x_s^{B_{si}}$	the reaction rate of the reaction $(C_i, C_j) \in \mathcal{R}$ at $x \in \mathbb{R}^n_{\geq 0}$
$R = [\cdots, R_{(i,j)}, \cdots]^\top_{(i,j) \in \mathcal{R}} : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^m_{\geq 0}$	the reaction rate functions
$\dot{x}(\tau) = B \cdot I_\kappa \cdot \Theta(x(\tau)) =$ $= B \cdot I \cdot R(x(\tau)) =$ $= S \cdot R(x(\tau))$	the ODE that describes the time evolution of the species concentration
$E_+ = \{x \in \mathbb{R}^n_+ \mid B \cdot I_\kappa \cdot \Theta(x) = 0\}$	the set of positive steady states

Table 2.2: Summary of the notations related to mass action systems.

Chapter 3

Mass action systems with $\delta = \delta^1 + \cdots + \delta^\ell$

In this brief chapter we have collected some results concerning the set of positive steady states of mass action systems that satisfy

$$\delta = \delta^1 + \cdots + \delta^\ell, \tag{3.1}$$

i.e., the deficiency of the whole network equals to the sum of the deficiencies of the linkage classes (see Section 2.7 for the definition and basic properties of the deficiency). In Section 3.1, we provide some well-known results that describe the structure of the set of positive steady states, while in Section 3.2 we present a result about the relation between the positive steady states of a mass action system and the positive steady states of the linkage classes of that mass action system. This latter result is also known (see [29, Subsection 8.2]), but we provide here another proof than the one in [29, Subsection 8.2]. The results presented in this chapter are interesting in themselves and we will also make use of them in Chapter 4.

Recall from Section 2.5 that the linkage classes of a mass action system are denoted by $(\mathcal{C}^1, \mathcal{R}^1)$, $(\mathcal{C}^2, \mathcal{R}^2), \ldots, (\mathcal{C}^\ell, \mathcal{R}^\ell)$. Also, we have introduced the notations $c^r = |\mathcal{C}^r|$ and $m^r = |\mathcal{R}^r|$ ($r \in \overline{1, \ell}$). As a preparation for Sections 3.1 and 3.2, let us consider the matrices B, $\widehat{B}$, S, I_κ and the vector $\Theta(x)$ (for $x \in \mathbb{R}^n_{\geq 0}$) in the block forms

$$\begin{aligned}
B &= [B^1, \ldots, B^\ell] \in \mathbb{R}^{n \times (\sum_{r=1}^\ell c^r)}, \\
\widehat{B} &= [\widehat{B}^1, \ldots, \widehat{B}^\ell] \in \mathbb{R}^{(n+\ell) \times (\sum_{r=1}^\ell c^r)}, \\
S &= [S^1, \ldots, S^\ell] \in \mathbb{R}^{n \times (\sum_{r=1}^\ell m^r)}, \\
I_\kappa &= \begin{bmatrix} I_\kappa^1 & & 0 \\ & \ddots & \\ 0 & & I_\kappa^\ell \end{bmatrix} \in \mathbb{R}^{(\sum_{r=1}^\ell c^r) \times (\sum_{r=1}^\ell c^r)}, \text{ and} \\
\Theta(x) &= \begin{bmatrix} \Theta^1(x) \\ \vdots \\ \Theta^\ell(x) \end{bmatrix} \in \mathbb{R}_{\geq 0}^{\sum_{r=1}^\ell c^r},
\end{aligned}$$

where $B^r \in \mathbb{R}^{n\times c^r}$, $\widehat{B}^r \in \mathbb{R}^{(n+\ell)\times c^r}$, $S^r \in \mathbb{R}^{n\times m^r}$, $I_\kappa^r \in \mathbb{R}^{c^r\times c^r}$, and $\Theta^r(x) \in \mathbb{R}^{c^r}_{\geq 0}$ correspond to the rth linkage class ($r \in \overline{1,\ell}$). Recall that f is defined by (2.10). For $r \in \overline{1,\ell}$ let us introduce the function $f^r : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^n$ by

$$f^r(x) = \sum_{(i,j)\in\mathcal{R}^r} \kappa_{ij} \prod_{s=1}^{n} x_s^{B_{si}} \cdot (B_{\cdot j} - B_{\cdot i}) \text{ for } x \in \mathbb{R}^n_{\geq 0}.$$

Thus, $f = f^1 + \cdots + f^\ell$ and $f^r = B^r \cdot I_\kappa^r \cdot \Theta^r$ ($r \in \overline{1,\ell}$). Also, for $r \in \overline{1,\ell}$ let us define E_+^r by

$$E_+^r = \{x \in \mathbb{R}^n_+ \mid B^r \cdot I_\kappa^r \cdot \Theta^r(x) = 0\},$$

i.e., E_+^r is the set of positive steady states of the mass action system associated to the rth linkage class of the original mass action system. Recall that we did not assume in Section 2.1 that each of the species has positive stoichiometric coefficient in at least complex. Thus, we can consider all the ℓ mass action systems associated to the linkage classes with state space $\mathbb{R}^n_{\geq 0}$ (even if there exists a linkage class in which not all the elements of $\{X_1, \ldots, X_n\}$ take part).

3.1 The structure of the set of positive steady states (provided that it is nonempty)

It is obvious that $E_+ \supseteq \cap_{r=1}^\ell E_+^r$ holds for all mass action systems. As a direct consequence of the following proposition, if (3.1) holds then we have $E_+ = \cap_{r=1}^\ell E_+^r$.

Proposition 3.1 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies* (3.1)*. Fix $x \in \mathbb{R}^n_{\geq 0}$. Then $f(x) = 0$ if and only if $f^1(x) = \cdots = f^\ell(x) = 0$.*

Proof Clearly, we have $f(x) \in \operatorname{ran} S$ and $f^1(x) \in \operatorname{ran} S^1, \ldots, f^\ell(x) \in \operatorname{ran} S^\ell$. Thus, Proposition 2.15 concludes the proof. $\square$

The following proposition tells us that once we have a positive steady state, certain other elements of $\mathbb{R}^n_+$ are also steady states. This result can be found in [29, Proposition 7.1] with basically the same proof as the one presented here.

Proposition 3.2 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies* (3.1)*. Assume that $E_+ \neq \emptyset$ and fix any $x^* \in E_+$. Then*

$$E_+ \supseteq \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}.$$

Proof For $i \in \overline{1,c}$ let us define the function $\pi_i : \mathbb{R}^n_{\geq 0} \times \mathbb{R}^n_+ \to \mathbb{R}_{\geq 0}$ by

$$\pi_i(x,y) = \prod_{s=1}^{n} \left(\frac{x_s}{y_s}\right)^{B_{si}} \quad ((x,y) \in \mathbb{R}^n_{\geq 0} \times \mathbb{R}^n_+).$$

Fix for the rest of this proof $x \in \mathbb{R}^n_+$ such that $\log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp$. Then

$$\langle B_{\cdot j} - B_{\cdot i}, \log(x) - \log(x^*)\rangle = \langle S_{\cdot,(i,j)}, \log(x) - \log(x^*)\rangle = 0$$

for all $(i,j) \in \mathcal{R}$. Or equivalently, $\pi_i(x,x^*) = \pi_j(x,x^*)$ for all $(i,j) \in \mathcal{R}$. Thus, the value of $\pi_i(x,x^*)$ depends only on the linkage class of the complex C_i. Denote this common value by π^r for the rth linkage class ($r \in \overline{1,\ell}$). Then

$$\begin{aligned} f(x) = \sum_{r=1}^{\ell} f^r(x) &= \sum_{r=1}^{\ell} \left(\sum_{(i,j)\in\mathcal{R}^r} \kappa_{ij} \prod_{s=1}^{n} x_s^{B_{si}} (B_{\cdot j} - B_{\cdot i}) \right) = \\ &= \sum_{r=1}^{\ell} \left(\sum_{(i,j)\in\mathcal{R}^r} \kappa_{ij} \left(\prod_{s=1}^{n} (x_s^*)^{B_{si}} \right) \pi_i(x,x^*)(B_{\cdot j} - B_{\cdot i}) \right) = \sum_{r=1}^{\ell} \pi^r f^r(x^*). \end{aligned} \tag{3.2}$$

Since $x^* \in E_+$, we have $f(x^*) = 0$. Hence, by Proposition 3.1, $f^r(x^*) = 0$ for all $r \in \overline{1,\ell}$. This concludes the proof, because then $f(x) = 0$ follows from (3.2). $\square$

The part (a) of the following lemma (which is not a CRNT-specific result) is a result of Horn and Jackson [43, Section 4]. A somewhat different proof than the one in [43] can be found in [29, Appendix B]. A more general version is proven in [54, Lemma IV.1], we present here that proof, but only in the special case we need. Part (b) of the following lemma is due to Sontag [54, Theorem 5].

Lemma 3.3 *Let $\mathcal{S}$ be a linear subspace of $\mathbb{R}^n$ and let $\mathcal{P} = (p+\mathcal{S}) \cap \mathbb{R}^n_{\geq 0}$ for some $p \in \mathbb{R}^n_+$. Fix $x^* \in \mathbb{R}^n_+$. Then*

(a) there exists a unique $x \in \mathcal{P} \cap \mathbb{R}^n_+$ such that $\log(x) - \log(x^*) \in \mathcal{S}^\perp$ and

(b) the set $\{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in \mathcal{S}^\perp\}$ is C^∞-diffeomorphic to $\mathbb{R}^{n-\operatorname{rank} S}$ (and hence, is connected).

Proof For $s \in \overline{1,n}$ define the function $L_s : \mathbb{R} \to \mathbb{R}$ by

$$L_s(y) = x_s^* e^y - p_s y \quad (y \in \mathbb{R}).$$

Then $\lim_{y\to\infty} L_s(y) = \infty$, $\lim_{y\to-\infty} L_s(y) = \infty$, and L_s is continuous. Hence, L_s is proper, that is, $\{y \in \mathbb{R} \mid L_s(y) \leq v\}$ is compact for each $v \in \mathbb{R}$. Define the function $Q : \mathbb{R}^n \to \mathbb{R}$ by

$$Q(y) = \sum_{s=1}^{n} L_s(y_s) \quad (y \in \mathbb{R}^n).$$

Note that Q is continuously differentiable. The function Q inherits the proper property from the functions L_s ($s \in \overline{1,n}$), because

$$\{y \in \mathbb{R}^n \mid Q(y) \leq w\} \subseteq \bigtimes_{s=1}^{n} \{y_s \in \mathbb{R} \mid L_s(y_s) \leq w - (n-1)M\},$$

where $M \in \mathbb{R}$ is any common lower bound for the functions L_s ($s \in \overline{1,n}$). Restricted to $\mathcal{S}^\perp$, Q is still proper, so it attains a minimum at some point $y^* \in \mathcal{S}^\perp$. The transpose of the gradient of Q at point $y^* \in \mathbb{R}^n$ must be orthogonal to $\mathcal{S}^\perp$ and hence

$$((\operatorname{grad} Q)(y^*))^\top = [x_1^* e^{y_1^*} - p_1, \ldots, x_n^* e^{y_n^*} - p_n]^\top = [x_1^* e^{y_1^*}, \ldots, x_n^* e^{y_n^*}]^\top - p \in (\mathcal{S}^\perp)^\perp = \mathcal{S}. \tag{3.3}$$

Pick $x \in \mathbb{R}^n_+$ such that $\log(x) = y^* + \log(x^*)$. Then $\log(x) - \log(x^*) = y^* \in \mathcal{S}^\perp$. Moreover, (3.3) shows that $x - p \in \mathcal{S}$. In other words, $x \in \mathcal{P} \cap \mathbb{R}^n_+$.

To prove (a), it remains to show the uniqueness part of the statement. Suppose that $x^1, x^2 \in \mathcal{P}\cap\mathbb{R}^n_+$ and $\log(x^1)-\log(x^*), \log(x^2)-\log(x^*) \in \mathcal{S}^\perp$. Then $x^1-x^2 \in \mathcal{S}$ and $\log(x^1)-\log(x^2) \in \mathcal{S}^\perp$. Since $\log : \mathbb{R}_+ \to \mathbb{R}$ is strictly increasing, $(a-b)(\log(a) - \log(b)) > 0$ for any $a, b \in \mathbb{R}_+$ distinct numbers. Thus

$$0 = \langle x^1 - x^2, \log(x^1) - \log(x^2)\rangle = \sum_{s=1}^{n} (x^1_s - x^2_s)(\log(x^1_s) - \log(x^2_s))$$

implies that $x^1_s = x^2_s$ for all $s \in \overline{1, n}$.

To show (b), define the (C^∞-diffeomorphism) $\Phi : \mathbb{R}^n \to \mathbb{R}^n_+$ by

$$\Phi(y) = [x^*_1 e^{y_1}, \ldots, x^*_n e^{y_n}]^\top$$

for $y \in \mathbb{R}^n$. We claim that $\Phi(\mathcal{S}^\perp) = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in \mathcal{S}^\perp\}$. Note that $x \in \Phi(\mathcal{S}^\perp)$ if and only if there exists a $y^* \in \mathcal{S}^\perp$ such that $\log(x^*) + y^* = \log(x)$, that is, if and only if $\log(x) - \log(x^*) \in \mathcal{S}^\perp$. The claim is therefore verified and (b) follows. (The connectedness follows from the fact that continuous image of a connected set is connected.) $\square$

Though the following corollary is not stated explicitly in [29], all its ingredients can be found there. The corollary provides a description of the set of positive steady states of mass action systems with (3.1).

Corollary 3.4 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies* (3.1)*. Assume that $E_+ \neq \emptyset$ and let $\mathcal{P}$ be a positive stoichiometric class such that $E_+ \cap \mathcal{P} \neq \emptyset$. For $x^* \in \mathbb{R}^n_+$ let $Q(x^*) = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$. Then*

$$E_+ = \bigcup^*_{x^* \in E_+ \cap \mathcal{P}} Q(x^*), \tag{3.4}$$

where the symbol $*$ next to $\bigcup$ stresses that if $x^{*,1}, x^{*,2} \in E_+ \cap \mathcal{P}$ and $x^{*,1} \neq x^{*,2}$ then $Q(x^{*,1}) \cap Q(x^{*,2}) = \emptyset$.

Proof Clearly, for all $x, x^* \in \mathbb{R}^n_+$ we have

$$x \in Q(x^*) \text{ if and only if } x^* \in Q(x). \tag{3.5}$$

Thus, if $x^{*,1}, x^{*,2} \in E_+ \cap \mathcal{P}$ and $x \in Q(x^{*,1}) \cap Q(x^{*,2})$ then $x^{*,1}, x^{*,2} \in Q(x)$. Hence, by Lemma 3.3, we have $x^{*,1} = x^{*,2}$. This shows that the union on the right hand side of (3.4) is indeed taken for disjoint sets.

The inclusion

$$E_+ \supseteq \bigcup^*_{x^* \in E_+ \cap \mathcal{P}} Q(x^*)$$

is a direct consequence of Proposition 3.2.

On the other hand, if $x \in E_+$ then, by Lemma 3.3, there exists a unique $x^* \in \mathcal{P} \cap Q(x)$. By Proposition 3.2, we have $x^* \in E_+$. Finally, by (3.5), we have $x \in Q(x^*)$. Thus, the inclusion

$$E_+ \subseteq \bigcup_{x^* \in E_+ \cap \mathcal{P}}^{*} Q(x^*)$$

also follows and this concludes the proof. $\square$

Corollary 3.5 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies* (3.1). *Assume that $E_+ \neq \emptyset$. Then*

(a) for all positive stoichiometric classes $\mathcal{P}$ and $\mathcal{P}'$ there exists a bijection between $E_+ \cap \mathcal{P}$ and $E_+ \cap \mathcal{P}'$ and

(b) if $E_+ \cap \mathcal{P}$ is finite for some positive stoichiometric class $\mathcal{P}$ then

(ba) $E_+ \cap \mathcal{P}'$ is finite for each positive stoichiometric class $\mathcal{P}'$ and

(bb) $|E_+ \cap \mathcal{P}'| = |E_+ \cap \mathcal{P}|$ for each positive stoichiometric class $\mathcal{P}'$.

Proof Statement (a) is a direct consequence of Lemma 3.3 and Corollary 3.4, while statements (ba) and (bb) are trivial consequences of (a). $\square$

Note that if $\ell = 1$ then (3.1) holds trivially. Thus, Proposition 3.2 and Corollaries 3.4 and 3.5 are applicable for all single linkage class mass action systems. (Note that Proposition 3.1 is a tautology in case $\ell = 1$, while Lemma 3.3 is not a CRNT-specific result.)

In order to illustrate the results presented in this section, consider the mass action system

$$\begin{tikzcd} 2X_1 + X_2 \arrow[r, "1"] & 3X_1 \arrow[d, "\varepsilon"] \\ 3X_2 \arrow[u, "\varepsilon"] & X_1 + 2X_2, \arrow[l, "1"'] \end{tikzcd} \tag{3.6}$$

where $\varepsilon > 0$ is a parameter and the numbers depicted next to the reactions are the rate coefficients (this example is taken from [43, Section 7]). The stoichiometric subspace of the reaction network is

$$\operatorname{ran} S = \operatorname{span}\left(\begin{bmatrix} 1 \\ -1 \end{bmatrix}\right).$$

Thus, the positive stoichiometric classes are the closed line segments in $\mathbb{R}^2_{\geq 0}$ that connect $[a, 0]^\top \in \mathbb{R}^2_{\geq 0}$ and $[0, a]^\top \in \mathbb{R}^2_{\geq 0}$ for some $a \in \mathbb{R}_+$ (a few of them are depicted in Figure 3.1). A short calculation shows that

$$E_+ = \left\{ x \in \mathbb{R}^2_+ \;\middle|\; x_1 = x_2 \text{ or } 2\varepsilon \left(\frac{x_1}{x_2}\right)^2 + (2\varepsilon - 1)\frac{x_1}{x_2} + 2\varepsilon = 0 \right\}.$$

Thus, another short calculation shows that for $0 < \varepsilon < 1/6$ we have

$$E_+ = \left\{ x \in \mathbb{R}^2_+ \;\middle|\; x_1 = x_2 \right\} \bigcup^* \left\{ x \in \mathbb{R}^2_+ \;\middle|\; x_1 = \frac{1 - 2\varepsilon + \sqrt{-12\varepsilon^2 - 4\varepsilon + 1}}{4\varepsilon}\, x_2 \right\} \bigcup^*$$
$$\bigcup^* \left\{ x \in \mathbb{R}^2_+ \;\middle|\; x_1 = \frac{1 - 2\varepsilon - \sqrt{-12\varepsilon^2 - 4\varepsilon + 1}}{4\varepsilon}\, x_2 \right\},$$

while for $\varepsilon \geq 1/6$ we have

$$E_+ = \left\{ x \in \mathbb{R}^2_+ \;\middle|\; x_1 = x_2 \right\}.$$

Hence, for $0 < \varepsilon < 1/6$ there are exactly 3 positive steady states in each positive stoichiometric class, while for $\varepsilon \geq 1/6$ there is exactly 1 positive steady state in each positive stoichiometric class. We have depicted E_+ for both of these cases in Figure 3.1. Let $\mathcal{P}$ be a positive stoichiometric class. Though stability properties are not examined in this thesis, we mention here that for $0 < \varepsilon < 1/6$ one of the positive steady states in $\mathcal{P}$ (the one "in the middle" on the picture on the left in Figure 3.1) is unstable, while the other two are locally asymptotically stable relative to $\mathcal{P}$. For $\varepsilon \geq 1/6$, the unique element of $E_+ \cap \mathcal{P}$ is globally asymptotically stable relative to $\mathcal{P}$.

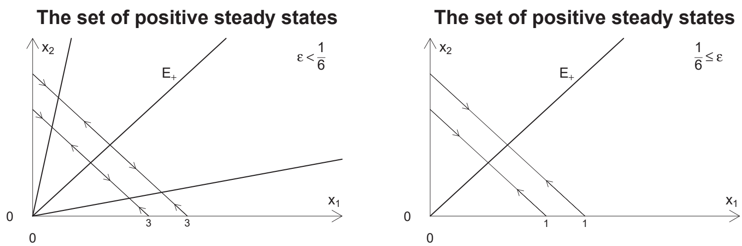


Figure 3.1: The set of positive steady states for two different ε's for the mass action system (3.6). The picture on the left is for $0 < \varepsilon < 1/6$, while the picture on the right is for $\varepsilon \geq 1/6$. The numbers under the depicted positive stoichiometric classes indicate the number of positive steady states in the respective positive stoichiometric class.

3.2 The non-emptiness of the set of positive steady states

Consider a mass action system that satisfies (3.1). As a consequence of Proposition 3.1, the positive steady states of the system are exactly those elements of $\mathbb{R}^n_+$ that are steady states of all the linkage classes at the same time. The following theorem, which is the main result of this chapter, states that if all the linkage classes have a positive steady state then they must have a common positive steady state as well. Thus, in case one needs to examine the non-emptiness of the set of positive steady states of a mass action system that satisfies (3.1), it suffices to deal with the non-emptiness of the set of positive steady states separately for the linkage classes. This result appears in [29, Lemma 8.2.3], the proof there relies on Proposition 3.2 above. The proof we present here is completely different, it relies on the Farkas' Lemma from linear algebra. See Appendix B for more details on the version of the Farkas' Lemma we need here. Beside the Farkas' Lemma, we use only Proposition 2.15. In that proposition, an equivalent formulation of (3.1) is given in terms of the matrix $\widehat{B} = [\widehat{B}^1, \ldots, \widehat{B}^\ell]$. The proof below of Theorem 3.6 also demonstrates that the matrix $\widehat{B}$ shows up naturally when investigating the set of positive steady states of a mass action system. We will use a similar technique in Chapters 4 and 5 while examining the set of positive steady states under some extra assumptions on the deficiency.

In the Deficiency-One Theorem it is assumed that (3.1) holds (see Theorem 4.2). Thus, we will use Theorem 3.6 below to prove the multiple linkage classes case of the Deficiency-One Theorem.

Theorem 3.6 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies* (3.1). *Then $E_+ \neq \emptyset$ if and only if $E_+^r \neq \emptyset$ for all $r \in \overline{1, \ell}$.*

Proof Assume first that $E_+ \neq \emptyset$ holds. It follows from Proposition 3.1 immediately that $E_+^r \neq \emptyset$ for all $r \in \overline{1, \ell}$.

Assume for the rest of this proof that $E_+^r \neq \emptyset$ for all $r \in \overline{1, \ell}$. Note that for fixed $r \in \overline{1, \ell}$ we have $x \in E_+^r$ if and only if

$$\text{there exists a } v^r \in \mathbb{R}_+^{c^r} \text{ such that } \Theta^r(x) = v^r \text{ and } B^r \cdot I_\kappa^r \cdot v^r = 0.$$

Since $\log(\Theta^r(x)) = (B^r)^\top \log(x)$ and $\log : \mathbb{R}_+^n \to \mathbb{R}^n$ is a bijection, we obtain that $E_+^r \neq \emptyset$ if and only if

$$\text{there exists a } v^r \in \mathbb{R}_+^{c^r} \text{ such that } \log(v^r) \in \operatorname{ran}(B^r)^\top \text{ and } B^r \cdot I_\kappa^r \cdot v^r = 0. \tag{3.7}$$

Let $\mathbf{1}^r$ be the vector in $\mathbb{R}^{c^r}$ with all coordinates being 1. Since $\operatorname{ran}(\widehat{B}^r)^\top = \operatorname{ran}[(B^r)^\top, \mathbf{1}^r]$ and for all $\gamma^r \in \mathbb{R}_+$ we have $\log(\gamma^r v^r) = \log(v^r) + \log(\gamma^r)\mathbf{1}^r$, we obtain that (3.7) is equivalent to

$$\text{there exists a } v^r \in \mathbb{R}_+^{c^r} \text{ such that } \log(v^r) \in \operatorname{ran}(\widehat{B}^r)^\top \text{ and } B^r \cdot I_\kappa^r \cdot v^r = 0.$$

Fix for the rest of this proof $v^1, \ldots, v^\ell$ such that $\log(v^r) \in \operatorname{ran}(\widehat{B}^r)^\top$ and $B^r \cdot I_\kappa^r \cdot v^r = 0$ for all $r \in \overline{1, \ell}$. By Proposition 2.15, we have $\operatorname{ran} \widehat{B} = \operatorname{ran} \widehat{B}^1 \oplus \operatorname{ran} \widehat{B}^2 \oplus \cdots \oplus \operatorname{ran} \widehat{B}^\ell$. Thus, a result of linear algebra, Corollary B.2 implies that there exist $u \in \mathbb{R}^n$ and $w \in \mathbb{R}^\ell$ such that

$$\begin{bmatrix} \log(v^1) \\ \vdots \\ \log(v^\ell) \end{bmatrix} = \begin{bmatrix} (\widehat{B}^1)^\top \\ \vdots \\ (\widehat{B}^\ell)^\top \end{bmatrix} \begin{bmatrix} u \\ w \end{bmatrix}. \tag{3.8}$$

Let $x \in \mathbb{R}^n_+$ and $\gamma^1, \dots, \gamma^\ell \in \mathbb{R}_+$ be such that $\log(x) = u$ and $-\log(\gamma^r) = w_r$ for all $r \in \overline{1,\ell}$. Then, by (3.8), for all $r \in \overline{1,\ell}$ and for all $i \in \mathcal{C}^r$ we have $\gamma^r v_i^r = \prod_{s=1}^n x_s^{B_{si}} = \Theta_i(x)$. Thus, $\Theta^r(x) = \gamma^r v^r$ and

$$B \cdot I_\kappa \cdot \Theta(x) = \sum_{r=1}^{\ell} B^r \cdot I_\kappa^r \cdot \Theta^r(x) = \sum_{r=1}^{\ell} \gamma^r \cdot B^r \cdot I_\kappa^r \cdot v^r = \sum_{r=1}^{\ell} \gamma^r \cdot 0 = 0.$$

Hence, $x \in E_+$, and thus, $E_+ \neq \emptyset$. $\square$

3.3 The acyclic directed graph of the implications

We have depicted below the acyclic directed graph of the implications of this chapter. For the organising principle of this directed graph, see Section 2.8.

$$\begin{tikzcd}
\text{P B.1} \arrow[d] & & \text{P 2.15} \arrow[dl] \arrow[dr] & & & \text{L 3.3} \arrow[d] \arrow[dd, bend left] \\
\text{C B.2} \arrow[r] & \text{T 3.6} & & \text{P 3.1} \arrow[r] & \text{P 3.2} \arrow[r] & \text{C 3.4} \arrow[d] \\
& & & & & \text{C 3.5}
\end{tikzcd}$$

Chapter 4

Generalisation of the Deficiency-One Theorem

Recall from Section 2.3 that the set of positive steady states of a mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ is

$$E_+ = \{x \in \mathbb{R}^n_+ \mid B \cdot I_\kappa \cdot \Theta(x) = 0\},$$

where B is the matrix of complexes, I_κ is the Laplacian of the labelled directed graph $(\mathcal{C}, \mathcal{R}, \kappa)$, and Θ is a function with its coordinate functions being monomials (see Section 2.3). Also, recall from Section 2.4 that the relevant way to look at the dynamics of a mass action system is to restrict that to a stoichiometric class. Thus, e.g. the existence, uniqueness, and finiteness of positive steady states should be asked with respect to a stoichiometric class. Also, stability properties of the positive steady states should be examined with respect to its stoichiometric class. The following classical theorem of Feinberg, Horn, and Jackson, called the *Deficiency-Zero Theorem*, answers these questions for deficiency-zero mass action systems (see [26, 27, 29, 31, 38, 43]).

Theorem 4.1 (Deficiency-Zero Theorem) *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies $\delta = 0$. Then*

(a) $E_+ \neq \emptyset$ if and only if $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ is weakly reversible,

(b) if $E_+ \neq \emptyset$ then $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$, and

(c) if $E_+ \neq \emptyset$ then the unique positive steady state in $\mathcal{P}$ is locally asymptotically stable with respect to $\mathcal{P}$ for each positive stoichiometric class $\mathcal{P}$.

Note that the asymptotic stability in Theorem 4.1 (c) is local. However, it is conjectured that all the trajectories starting in $\mathcal{P} \cap \mathbb{R}^n_+$ converge to the unique positive steady state in $\mathcal{P}$. This global stability result was asserted in [43], while its proof was retracted in [42]. Recently, much effort has been dedicated to prove this conjecture, which was given the name *Global Attractor Conjecture* (see e.g. [1, 3, 5, 6, 16, 17, 22, 49, 54]).

Since the deficiency is a nonnegative number and $\delta^1 + \cdots + \delta^\ell \leq \delta$ holds generally (see Section 2.7), we obtain that all deficiency-zero reaction networks satisfy $\delta^1 + \cdots + \delta^\ell = \delta$. Thus, the also classical *Deficiency-One Theorem* (due to Feinberg [25, 27, 29]) generalises some of the statements of the Deficiency-Zero Theorem.

Theorem 4.2 (Deficiency-One Theorem) *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies*

(i) $\delta^r \leq 1$ for all $r \in \overline{1, \ell}$,

(ii) $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$, and

(iii) $\ell = t$ (i.e., each of the linkage classes contains only one terminal strong linkage class).

Then

(a) if $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ is weakly reversible then $E_+ \neq \emptyset$ and

(b) if $E_+ \neq \emptyset$ then $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$.

Unlike the Deficiency-Zero Theorem, the Deficiency-One Theorem does not state anything about the stability of the unique positive steady state. Actually, the local asymptotic stability does not remain valid in general. It is mentioned both in [25] and [29] that there exist rate coefficients for the reaction network

$$\begin{tikzcd}
 & X_1 \arrow[r, shift left] \arrow[d, shift left] & 2X_1 \arrow[l, shift left] \\
X_1 + X_2 \arrow[r, shift left] & X_3 \arrow[l, shift left] \arrow[u, shift left] \arrow[r, shift left] & X_2 \arrow[l, shift left]
\end{tikzcd} \tag{4.1}$$

such that the unique positive steady state of the resulting mass action system is unstable (see [25, (3.25)] and [29, (4.12)]). (It is apparent that (4.1) is a weakly reversible single linkage class deficiency-one reaction network with stoichiometric subspace $\mathbb{R}^3$. Thus, there is only one positive stoichiometric class, the nonnegative orthant $\mathbb{R}^3_{\geq 0}$ itself. Therefore, the Deficiency-One Theorem implies that $|E_+| = 1$.)

Beyond the lack of the stability result in the Deficiency-One Theorem, the other difference is that the Deficiency-One Theorem does not state anything about the non-emptiness of the set of positive steady states for mass action systems, which are not weakly reversible. A short calculation shows that for the mass action system

$$2X_1 \xrightarrow{\kappa_{32}} X_1 + X_2 \underset{\kappa_{12}}{\overset{\kappa_{21}}{\rightleftharpoons}} 2X_2 \tag{4.2}$$

we have $E_+ \neq \emptyset$ for all $\kappa_{12}, \kappa_{21}, \kappa_{32} > 0$. For the mass action system

$$2X_1 \xrightarrow{\kappa_{32}} X_1 + X_2 \xrightarrow{\kappa_{21}} 2X_2 \tag{4.3}$$

we obtain that $E_+ = \emptyset$ for all $\kappa_{21}, \kappa_{32} > 0$. Finally, for the mass action system

$$2X_1 \underset{\kappa_{23}}{\overset{\kappa_{32}}{\rightleftarrows}} X_1 + X_2 \xrightarrow{\kappa_{21}} 2X_2 \tag{4.4}$$

we have $E_+ \neq \emptyset$ if $\kappa_{32} > 0$ and $0 < \kappa_{21} < \kappa_{23}$, while we have $E_+ = \emptyset$ if $\kappa_{32} > 0$ and $0 < \kappa_{23} \leq \kappa_{21}$. Clearly, all the above three examples are of deficiency-one. Thus, given a single linkage class deficiency-one reaction network that is not weakly reversible, the following three different kind of phenomena can occur while rate coefficients are assigned to that:

- $E_+ \neq \emptyset$ for all κ,
- $E_+ = \emptyset$ for all κ, and
- the non-emptiness of E_+ depends on κ (i.e., there exists a κ such that $E_+ \neq \emptyset$ and there also exists a κ such that $E_+ = \emptyset$).

The main result of this chapter is that we provide an equivalent condition to the non-emptiness of the set of positive steady states for single linkage class deficiency-one mass action systems that are not weakly reversible (see Theorem 4.13). It turns out that a trivially obtained necessary condition also serves as a sufficient condition to the non-emptiness of E_+. The proof of the sufficiency is similar to the proof of the weakly reversible case. This result was published in [11] and [12].

Before the summary of the rest of this chapter, we provide some results that are not related to the notion of the deficiency, but will be used during the proofs of the Deficiency-Zero- and Deficiency-One Theorems. Rather, these are general facts about reaction networks. Proposition 4.3 below makes a connection between $\ker \widehat{B}^\top$ and $(\operatorname{ran} S)^\perp$, which is the key to Corollaries 4.4 and 4.5 below. As we already saw in the proof of Theorem 3.6, the matrix $\widehat{B}$ shows up naturally when investigating the set of positive steady states of a mass action system. While proving the single linkage class cases of Theorems 4.1 and 4.2 in Section 4.1 and Subsection 4.3.1, respectively, we will again experience that $\widehat{B}$ shows up in a natural way. Corollary 4.5 below will also be used in Chapter 5.

Proposition 4.3 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Denote by n the number of species and by ℓ the number of linkage classes. Let $\widehat{B}$ be as in (2.16) and let S be the stoichiometric matrix. Let $\mathrm{Pr}_1 : \mathbb{R}^n \times \mathbb{R}^\ell \to \mathbb{R}^n$ be the first projection map, i.e., $\mathrm{Pr}_1\, v = v^1$ for $v = \begin{bmatrix} v^1 \\ v^2 \end{bmatrix} \in \mathbb{R}^n \times \mathbb{R}^\ell$. Then $\mathrm{Pr}_1|_{\ker \widehat{B}^\top}$ is a bijection between $\ker \widehat{B}^\top$ and $(\operatorname{ran} S)^\perp$.*

Proof First note that

$$\dim \ker \widehat{B}^\top = \dim \ker \widehat{B} + n + \ell - c = \delta + n + \ell - c = n - \operatorname{rank} S = \dim((\operatorname{ran} S)^\perp).$$

Hence, it suffices to prove that if $w \in (\operatorname{ran} S)^\perp$ then there exists a $v \in \ker \widehat{B}^\top$ such that $\mathrm{Pr}_1\, v = w$. For this purpose, let $w \in (\operatorname{ran} S)^\perp$. This means that $\langle B_{\cdot j} - B_{\cdot i}, w \rangle = 0$ for all $(i, j) \in \mathcal{R}$. Therefore,

$\langle B_{\cdot i}, w\rangle$ depends only on the linkage class of $i \in \mathcal{C}$. Denote this common value by ξ_r for the rth linkage class ($r \in \overline{1,\ell}$). Let us define $v \in \mathbb{R}^n \times \mathbb{R}^\ell$ by $v = [w^\top, -\xi_1, \ldots, -\xi_\ell]^\top$. Clearly,

$$\widehat{B}^\top v = B^\top w + L \begin{bmatrix} -\xi_1 \\ \vdots \\ -\xi_\ell \end{bmatrix} = 0$$

(i.e., $v \in \ker \widehat{B}^\top$) and $\Pr_1 v = w$. $\square$

Corollary 4.4 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Denote by n the number of species and by ℓ the number of linkage classes. Let $\widehat{B}$ be as in (2.16) and let S be the stoichiometric matrix. Fix $w \in \operatorname{ran} \widehat{B}^\top$ and $x^* \in \mathbb{R}^n_+$ such that*

$$\textit{there exists a } \gamma^* \in \mathbb{R}^\ell_+ \textit{ such that } \widehat{B}^\top \begin{bmatrix} \log(x^*) \\ -\log(\gamma^*) \end{bmatrix} = w.$$

Then for $x \in \mathbb{R}^n_+$ the following are equivalent.

(A) There exists a $\gamma \in \mathbb{R}^\ell_+$ such that $\widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = w.$

(B) The vector $\log(x) - \log(x^*)$ is in $(\operatorname{ran} S)^\perp$.

Proof The equivalence is an immediate consequence of Proposition 4.3 and the fact that $-\log : \mathbb{R}^\ell_+ \to \mathbb{R}^\ell$ is a bijection. $\square$

Corollary 4.5 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network. Denote by n the number of species and by ℓ the number of linkage classes. Let $\widehat{B}$ be as in (2.16), let S be the stoichiometric matrix, and fix $w \in \operatorname{ran} \widehat{B}^\top$. Then for all $q \in \mathbb{R}^n_+$ there exists a unique $(x, \gamma) \in \mathbb{R}^n_+ \times \mathbb{R}^\ell_+$ such that*

$$x \in q + \operatorname{ran} S \textit{ and } \widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = w.$$

Proof The statement is a direct consequence of Lemma 3.3 and Corollary 4.4. $\square$

The rest of this chapter is organised as follows. In Section 4.1 we prove Theorem 4.1 (a) and (b) for the single linkage class case (we do not deal with the stability properties of the positive steady states in this thesis). In Section 4.2 we prove some properties of certain power functions (the results in this section are not strongly related to CRNT). Based on Section 4.2, we prove Theorem 4.2 for the single linkage class case in Section 4.3. Once we have in hand the not CRNT-specific results of Section 4.2, it will become apparent that the proof of the existence and uniqueness of positive steady states for weakly reversible single linkage class deficiency-one mass action systems is almost the same as for the deficiency-zero case. This recognition also led us to the treatment of the non weakly reversible single linkage class deficiency-one case. It turns out that a trivially obtained necessary condition (which condition is not deficiency-specific at all) is also sufficient for the existence and uniqueness of positive steady states (see Subsection 4.3.2). With some minor differences, the proof of the sufficiency follows the line of the proof of the weakly reversible case. Based on Chapter 3, we prove all the statements of Theorem 4.2 in Section 4.4. We conclude this chapter by Section 4.5, in which we present additional material to Section 4.2. However, the findings of Section 4.5 are not used during the proofs of the main results of this thesis.

4.1 Proof of the Deficiency-Zero Theorem: single linkage class

We prove in this section Theorem 4.1 (a) and (b) for the single linkage class case. As we will see in Section 4.3, the proof of Theorem 4.6 presented below can be adopted to the deficiency-one case with minor modifications.

Theorem 4.6 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies $\ell = 1$ and $\delta = 0$. Then*

(a) $E_+ \neq \emptyset$ if and only if $(\mathcal{C}, \mathcal{R})$ is strongly connected,

(b) if $E_+ \neq \emptyset$ and $x^* \in E_+$ then $E_+ = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$, and

(c) if $E_+ \neq \emptyset$ then $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$.

Proof Since $\delta = 0$, we have $\ker B \cap \operatorname{ran} I = \{0\}$ (see Proposition 2.10). Hence, it follows that $E_+ = \{x \in \mathbb{R}^n_+ \mid I \cdot R(x) = 0\} = \{x \in \mathbb{R}^n_+ \mid I_\kappa \cdot \Theta(x) = 0\}$. If $(\mathcal{C}, \mathcal{R})$ is not strongly connected then each element of $\ker I_\kappa$ has at least one zero coordinate. Indeed, those coordinates that are corresponding to complexes that are not in the terminal strong linkage classes are necessarily zero (see Lemma 2.5 for a description of the kernel of I_κ). Since $\Theta(x) \in \mathbb{R}^c_+$ for all $x \in \mathbb{R}^n_+$, clearly $E_+ = \emptyset$ follows in this case.

Assume for the rest of this proof that $(\mathcal{C}, \mathcal{R})$ is strongly connected. By Lemma 2.5, there exists a $y \in \mathbb{R}^c_+$ such that $\ker I_\kappa = \operatorname{span}(y)$. Since $\Theta(x) \in \mathbb{R}^c_+$ for all $x \in \mathbb{R}^n_+$, to find an element in E_+ is equivalent to find some $\gamma \in \mathbb{R}_+$ and $x \in \mathbb{R}^n_+$ such that $\gamma y = \Theta(x)$. Taking the logarithm of the last equality coordinatewise yields $\log(\gamma)e + \log(y) = B^\top \cdot \log(x)$, where e is the vector in $\mathbb{R}^c$ with all coordinates being 1. Thus, by dropping $\log(\gamma)e$ to the other side, a vector $x \in \mathbb{R}^n_+$ is also in E_+ if and only if

$$\text{there exists a } \gamma \in \mathbb{R}_+ \text{ such that } \log(y) = \widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix}.$$

Since $\dim \ker \widehat{B} = \delta = 0$, the matrix $\widehat{B}^\top$ has full range. Hence, $\log(y)$ is in $\operatorname{ran} \widehat{B}^\top$. Since $\log : \mathbb{R}^n_+ \to \mathbb{R}^n$ and $-\log : \mathbb{R}_+ \to \mathbb{R}$ are bijections, we directly obtain that $E_+ \neq \emptyset$. This concludes the proof of (a).

Statements (b) and (c) follow immediately from Corollaries 4.4 and 4.5, respectively. □

4.2 A lemma to the proof of the Deficiency-One Theorem

In the proof of Theorem 4.6, there was a vector y from the kernel of I_κ that played a role. As we will see in Section 4.3, for the deficiency-one case there will be a vector $\overline{y}$ from the kernel of I_κ and also a vector y^* for which $I_\kappa y^* = h$ holds, where h is a nonzero vector from the one-dimensional linear space $\ker B \cap \operatorname{ran} I_\kappa$ (recall from Section 2.7 that for networks with $\ell = t$, the deficiency equals to the dimension of the linear space $\ker B \cap \operatorname{ran} I_\kappa$). It will turn out during the proofs of the main results of Section 4.3 that the power function

$$p(\beta) = \prod_{i \in \mathcal{C}} (\beta y_i^* + \overline{y}_i)^{h_i}$$

plays a crucial role with respect to the existence and uniqueness of the positive steady states. Thus, the aim of this section is to prove Corollary 4.10 below, which is about certain properties of p. We will be interested in the limits of p at the endpoints of its domain. Also, the monotonicity properties of p are relevant, and therefore we will examine the sign of the derivative of p. The results then play a crucial role in Section 4.3 and Chapter 5. Having in hand Corollary 4.10, one can prove the Deficiency-One Theorem using a very similar argument as in the proof the Deficiency-Zero Theorem (see the proofs of Theorems 4.6 and 4.11). Also, the extension of the Deficiency-One Theorem to the non weakly reversible case can be proven in a similar way as Theorems 4.6 and 4.11 (see Theorem 4.13 for this extension; this result is the main contribution of the author of this thesis to the Deficiency-One Theorem). Though we will apply Corollary 4.10 in situations that are related to the fact that the deficiency of a mass action system equals to 1, we emphasise that the results of this section may be applied for cases when the deficiency is higher than 1. Since the quantities appearing in the definition of p are related to each other via the Laplacian (and there is nothing to do with the matrix of complexes), the achievements of this section may be applied in other areas than CRNT.

In this section, h will denote an element of $\operatorname{ran} I_\kappa$. Since the sum of the rows of the matrix I_κ is the zero vector in $\mathbb{R}^c$, we have

$$\sum_{i=1}^{c} h_i = 0. \tag{4.5}$$

As a preparation for Corollary 4.10, we prove Lemma 4.7 and its consequence, Corollary 4.9 below. Lemma 4.7 (a) and (b) below are essentially the same as [29, Lemma 6.2.1], however, in a somewhat different language.

Lemma 4.7 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system with only one terminal strong linkage class (consequently, there is only one linkage class). Denote by $\mathcal{C}'$ the vertex set of the terminal strong linkage class and let $c = |\mathcal{C}|$ and $c' = |\mathcal{C}'|$ (thus, $1 \le c' \le c$). Assume that the complexes are labelled such that $\mathcal{C}' = \{C_1, C_2, \ldots, C_{c'}\}$. Let I_κ be as in* (2.8) *and suppose that $\overline{y} \in \mathbb{R}^{\mathcal{C}}_{\ge 0}$,*

$y^* \in \mathbb{R}^c_{\geq 0}$, and $h \in \mathbb{R}^c \backslash \{0\}$ are such that $I_\kappa \overline{y} = 0$, $I_\kappa y^* = h$,

$$\text{for all } j \in \mathcal{C} \text{ we have } \overline{y}_j > 0 \text{ if and only if } j \in \mathcal{C}', \tag{4.6}$$

$$\text{for all } j \in \mathcal{C}\backslash\mathcal{C}' \text{ we have } y^*_j > 0, \text{ and} \tag{4.7}$$

$$\text{there exists a } j \in \mathcal{C}' \text{ such that } y^*_j = 0. \tag{4.8}$$

Assume also that

$$0 = \frac{y^*_1}{\overline{y}_1} \leq \frac{y^*_2}{\overline{y}_2} \leq \cdots \leq \frac{y^*_{c'}}{\overline{y}_{c'}}. \tag{4.9}$$

Then

(a) for all $M \in \overline{1, c'}$ we have

$$\sum_{i=1}^{M} h_i \geq 0,$$

(b) if $M \in \overline{1, c'}$ is such that $M + 1 \leq c$ and $\frac{y^*_M}{\overline{y}_M} \overline{y}_{M+1} < y^*_{M+1}$ then

$$\sum_{i=1}^{M} h_i > 0,$$

(c) if $(\mathcal{C}, \mathcal{R})$ is strongly connected (i.e., $c' = c$) then there exist $1 \leq k \leq l < c - 1$ such that

$$0 = \frac{y^*_1}{\overline{y}_1} = \cdots = \frac{y^*_k}{\overline{y}_k} < \frac{y^*_{k+1}}{\overline{y}_{k+1}} \leq \cdots \leq \frac{y^*_l}{\overline{y}_l} < \frac{y^*_{l+1}}{\overline{y}_{l+1}} = \cdots = \frac{y^*_c}{\overline{y}_c}, \text{ and}$$

(d) if $(\mathcal{C}, \mathcal{R})$ is not *strongly connected (i.e., $c' < c$) then*

(da) we have $\frac{y^*_{c'}}{\overline{y}_{c'}} \overline{y}_{c'+1} < y^*_{c'+1}$ and

(db) there exists a $1 \leq k \leq c'$ such that

$$0 = \frac{y^*_1}{\overline{y}_1} = \cdots = \frac{y^*_k}{\overline{y}_k} < \frac{y^*_{k+1}}{\overline{y}_{k+1}} \leq \cdots \leq \frac{y^*_{c'}}{\overline{y}_{c'}}.$$

Remark 4.8 Before proving Lemma 4.7, we make some comments about the existence of $\overline{y}$, y^*, and h that satisfy the suppositions of Lemma 4.7.

Assume first that $(\mathcal{C}, \mathcal{R})$ is strongly connected. Clearly, if $\overline{y} \in \mathbb{R}^c_{\geq 0}$ and $y^* \in \mathbb{R}^c_{\geq 0}$ then (4.6), (4.7), and (4.8) together are equivalent to $\overline{y} \in \mathbb{R}^c_+$ and $y^* \in \mathrm{bd}(\mathbb{R}^c_+)$, where $\mathrm{bd}(\mathbb{R}^c_+)$ denotes the boundary of $\mathbb{R}^c_+$. By Lemma 2.5, there exists a $\overline{y} \in \mathbb{R}^c_+$ such that $I_\kappa \overline{y} = 0$. Once $0 \neq h \in \operatorname{ran} I_\kappa$ is fixed, the existence of $y^* \in \mathrm{bd}(\mathbb{R}^c_+)$ such that $I_\kappa y^* = h$ is, again, guaranteed by Lemma 2.5. To see that such a y^* indeed exists, let y be any vector in $\mathbb{R}^c$ such that $I_\kappa y = h$. Also, let $\lambda = \max\{-y_i/\overline{y}_i \mid i \in \mathcal{C}\}$ and let $y^* = y + \lambda \overline{y}$. With this, $y^* \in \mathrm{bd}(\mathbb{R}^c_+)$ and $I_\kappa y^* = h$. In fact, once h is fixed, the vector y^* with the above requirements is unique.

Assume now that $(\mathcal{C}, \mathcal{R})$ is not strongly connected. Then, by Lemma 2.5, there exists a $\overline{y} \in \mathbb{R}^c_{\geq 0}$ such that $I_\kappa \overline{y} = 0$ and (4.6) hold. Note that once $0 \neq h \in \operatorname{ran} I_\kappa$ is fixed and $y, \widetilde{y} \in \mathbb{R}^c$

are such that $I_\kappa y = I_\kappa \widetilde{y} = h$ then $y_i = \widetilde{y}_i$ for all $i \in \mathcal{C}\setminus\mathcal{C}'$. Indeed, the key to this is that I_κ is block triangular and the submatrix of I_κ with rows and columns corresponding to $\mathcal{C}\setminus\mathcal{C}'$ is invertible (see Lemma 2.5). Thus, if $y \in \mathbb{R}^c$ is such that $I_\kappa y = h$ then the value of y_i is determined by h for all $i \in \mathcal{C}\setminus\mathcal{C}'$. Consequently, for the existence of $y^* \in \mathbb{R}^c_{\geq 0}$ such that $I_\kappa y = h$ and (4.7) hold, it is necessary that these values (which are determined by h) are positive. Once this necessary condition holds, a similar argument as in the previous paragraph for the strongly connected case shows that this is also sufficient for the existence of $y^* \in \mathbb{R}^c_{\geq 0}$ such that $I_\kappa y = h$, (4.7), and (4.8) hold. In fact, once h is fixed, the vector y^* with the above requirements is unique. □

Proof of Lemma 4.7 The key to prove (a) and (b) is Proposition 2.3. Let us define $\overline{z} : \mathcal{R} \to \mathbb{R}$ and $z^* : \mathcal{R} \to \mathbb{R}$ by $\overline{z}_{(i,j)} = \kappa_{ij}\overline{y}_i$ and $z^*_{(i,j)} = \kappa_{ij}y^*_i$ ($(i,j) \in \mathcal{R}$), respectively.

Fix $M \in \overline{1,c'}$ and let $\widetilde{\mathcal{C}} = \{C_1, \ldots, C_M\}$. Taking into account (4.6) and (4.9), we have

$$\begin{aligned} &\frac{y^*_M}{\overline{y}_M}\overline{y}_i \leq y^*_i \text{ for all } (i,j) \in \varrho^{\mathrm{in}}(\widetilde{\mathcal{C}}) \text{ and} \\ &\frac{y^*_M}{\overline{y}_M}\overline{y}_i \geq y^*_i \text{ for all } (i,j) \in \varrho^{\mathrm{out}}(\widetilde{\mathcal{C}}). \end{aligned} \tag{4.10}$$

Thus, by Proposition 2.3 and the equalities $I_\kappa \overline{y} = 0$ and $I_\kappa y^* = h$, we obtain

$$\begin{aligned} \sum_{i=1}^{M} h_i &= \sum_{i=1}^{M} (I_\kappa y^*)_i = \mathrm{excess}_{z^*}(\widetilde{\mathcal{C}}) = \\ &= \left(\sum_{(i,j)\in\varrho^{\mathrm{in}}(\widetilde{\mathcal{C}})} \kappa_{ij} y^*_i\right) - \left(\sum_{(i,j)\in\varrho^{\mathrm{out}}(\widetilde{\mathcal{C}})} \kappa_{ij} y^*_i\right) \overset{(4.10)}{\geq} \\ &\overset{(4.10)}{\geq} \frac{y^*_M}{\overline{y}_M}\left[\left(\sum_{(i,j)\in\varrho^{\mathrm{in}}(\widetilde{\mathcal{C}})} \kappa_{ij}\overline{y}_i\right) - \left(\sum_{(i,j)\in\varrho^{\mathrm{out}}(\widetilde{\mathcal{C}})} \kappa_{ij}\overline{y}_i\right)\right] = \\ &= \frac{y^*_M}{\overline{y}_M}\mathrm{excess}_{\overline{z}}(\widetilde{\mathcal{C}}) = \frac{y^*_M}{\overline{y}_M}\sum_{i=1}^{M}(I_\kappa\overline{y})_i = \frac{y^*_M}{\overline{y}_M}\sum_{i=1}^{M} 0 = 0, \end{aligned} \tag{4.11}$$

which proves (a). To prove (b), fix $M \in \overline{1,c'}$ such that $M+1 \leq c$ and

$$\frac{y^*_M}{\overline{y}_M}\overline{y}_{M+1} < y^*_{M+1}. \tag{4.12}$$

At this point, we distinguish between two cases. On the one hand, if $M < c'$ then there exist i and j such that $1 \leq i \leq M < M+1 \leq j \leq c'$ and $\kappa_{ji} > 0$ (because the directed graph $(\mathcal{C}', \mathcal{R} \cap (\mathcal{C}' \times \mathcal{C}'))$ is strongly connected). Thus, by (4.9) and (4.12), we obtain strict inequality in the only inequality in (4.11). On the other hand, if $M = c'$ (and therefore $c' < c$) then there exist i and j such that $i \in \mathcal{C}'$ and $j \in \mathcal{C}\setminus\mathcal{C}'$ and $\kappa_{ji} > 0$ (because the directed graph $(\mathcal{C}, \mathcal{R})$ is weakly connected and $\varrho^{\mathrm{in}}(\mathcal{C}') \neq \emptyset$). Since $y^*_j > 0$ and $\overline{y}_j = 0$ (see (4.6) and (4.7)), again, by (4.9) and (4.12), we obtain strict inequality in the only inequality in (4.11). This concludes the proof of (b).

In statement (c), the case $k = l$ refers to the possibility that the fractions in (4.9) take only two different values. To prove (c), we need to show that it is impossible that all the fractions in

(4.9) are equal. So suppose by contradiction that $\frac{y_1^*}{\overline{y}_1} = \cdots = \frac{y_c^*}{\overline{y}_c}$ holds. Then $y^* = \lambda \overline{y}$ for some $\lambda \in \mathbb{R}$. However, then $0 \neq h = I_\kappa y^* = \lambda I_\kappa \overline{y} = 0$, contradiction.

To prove (da), it suffices to note that $\overline{y}_{c'} > 0$, $\overline{y}_{c'+1} = 0$ (see (4.6)), and $y^*_{c'+1} > 0$ (see (4.7)). Note that in (db) the case $k = c'$ refers to the possibility of $y_1^* = \cdots = y_{c'}^* = 0$. Therefore, (db) holds trivially, it is recorded in this lemma for further reference. □

The following corollary will be the key while investigating the sign of the derivative of the power function in Corollary 4.10.

Corollary 4.9 *In addition to the assumptions of Lemma 4.7, let* $(v_i)_{i=1}^c \subseteq \mathbb{R}$ *be a sequence such that*

$$v_1 \leq v_2 \leq \cdots \leq v_c. \tag{4.13}$$

Then

(a) if $(\mathcal{C}, \mathcal{R})$ *is strongly connected and for all* $M \in \overline{1, c-1}$ *we have*

$$\operatorname{sgn}(v_{M+1} - v_M) = \operatorname{sgn}\left(\frac{y^*_{M+1}}{\overline{y}_{M+1}} - \frac{y^*_M}{\overline{y}_M}\right) \tag{4.14}$$

then $\sum_{i=1}^c h_i v_i < 0$ *and*

(b) if $(\mathcal{C}, \mathcal{R})$ *is* not *strongly connected and*

$$v_1 \leq v_2 \leq \cdots \leq v_{c'} < v_{c'+1} = v_{c'+2} = \cdots = v_c. \tag{4.15}$$

then, again, $\sum_{i=1}^c h_i v_i < 0$.

Proof Note that

$$\sum_{i=1}^c h_i v_i = \left[\sum_{M=1}^{c-1}\left(\sum_{i=1}^M h_i\right)(v_M - v_{M+1})\right] + \left(\sum_{i=1}^c h_i\right) v_c. \tag{4.16}$$

Since $\sum_{i=1}^c h_i = 0$ (see (4.5)), the second term on the right hand side of (4.16) vanishes. (The idea of considering $\sum_{i=1}^c h_i v_i$ as in (4.16) is taken from [29, (6.2.12)].)

To prove (a), note that $\sum_{i=1}^M h_i \geq 0$ and $v_M - v_{M+1} \leq 0$ for all $M \in \overline{1, c-1}$ (see Lemma 4.7 (a) and (4.13)). Hence, we have $\sum_{i=1}^c h_i v_i \leq 0$. Let k be as in Lemma 4.7 (c). Lemma 4.7 (b) and (4.14) then concludes the proof of (a).

It is left to prove (b). By (4.15) and (4.16) we have

$$\sum_{i=1}^c h_i v_i = \left[\sum_{M=1}^{c'}\left(\sum_{i=1}^M h_i\right)(v_M - v_{M+1})\right].$$

Again, by Lemma 4.7 (a) and (4.13), we obtain that $\sum_{i=1}^c h_i v_i \leq 0$. Lemma 4.7 (b) and (da) and the fact that $v_{c'} < v_{c'+1}$ concludes the proof of (b). □

We are now in the position to state and prove the main result of this section, which deals with some qualitative properties of a power function. We examine the limits of this function at the endpoints of its domain. Also, the sign of its derivative is obtained.

Corollary 4.10 *In addition to the assumptions of Lemma 4.7, let us define $\beta^* \in \mathbb{R}$ and $p : (\beta^*, \infty) \to \mathbb{R}_+$ by*

$$\beta^* = \max\left\{ -\frac{\overline{y}_i}{y_i^*} \;\middle|\; i \in \mathcal{C} \text{ and } y_i^* > 0 \right\} \text{ and}$$
$$p(\beta) = \prod_{i \in \mathcal{C}} (\beta y_i^* + \overline{y}_i)^{h_i} \quad (\beta \in (\beta^*, \infty)),$$

respectively. Then

$$\lim_{\beta \to \beta^* + 0} p(\beta) = \infty, \tag{4.17}$$

$$\lim_{\beta \to \infty} p(\beta) = 0, \tag{4.18}$$

$$\partial p < 0 \text{ on } (\beta^*, \infty), \text{ and} \tag{4.19}$$

$$p : (\beta^*, \infty) \to \mathbb{R}_+ \text{ is a bijection.} \tag{4.20}$$

Proof Clearly, once we have established (4.17), (4.18), and (4.19), the statement in (4.20) follows immediately.

To obtain the limit of p at ∞, one needs to have the sign of

$$\sum_{\substack{i \in \mathcal{C} \\ y_i^* > 0}} h_i.$$

Let k be as in

$$\begin{cases} \text{Lemma 4.7 } (c), & \text{if } (\mathcal{C}, \mathcal{R}) \text{ is strongly connected,} \\ \text{Lemma 4.7 } (db), & \text{if } (\mathcal{C}, \mathcal{R}) \text{ is } \textit{not} \text{ strongly connected.} \end{cases}$$

In both cases, we have

$$\sum_{\substack{i \in \mathcal{C} \\ y_i^* > 0}} h_i = \sum_{i=k+1}^{c} \stackrel{(4.5)}{=} -\sum_{i=1}^{k} h_i < 0, \tag{4.21}$$

where we used Lemma 4.7 (b) (in case $k = c'$ in the "not strongly connected" case then we also need to take into account Lemma 4.7 (da)). This proves (4.18).

Similarly, to obtain the right limit of p at β^*, one needs to have the sign of

$$\sum_{\substack{i \in \mathcal{C} \\ y_i^* > 0 \\ -\overline{y}_i / y_i^* = \beta^*}} h_i, \tag{4.22}$$

which equals to

$$\begin{cases} \sum_{i=l+1}^{c} h_i, & \text{if } (\mathcal{C}, \mathcal{R}) \text{ is strongly connected,} \\ \sum_{i \in \mathcal{C} \setminus \mathcal{C}'} h_i, & \text{if } (\mathcal{C}, \mathcal{R}) \text{ is } \textit{not} \text{ strongly connected,} \end{cases}$$

where l is as in Lemma 4.7 (c). In both cases, similarly as in (4.21), we obtain that the sum in (4.22) is negative, which proves (4.17).

It remains to show (4.19). Note that

$$(\partial p)(\beta) = p(\beta) \sum_{i=1}^{c} h_i \frac{y_i^*}{\beta y_i^* + \overline{y}_i} \text{ for all } \beta \in (\beta^*, \infty). \tag{4.23}$$

Let

$$v_i(\beta) = \frac{y_i^*}{\beta y_i^* + \overline{y}_i} \quad (i \in \mathcal{C}, \beta \in (\beta^*, \infty)).$$

A short calculation shows that

$$\operatorname{sgn}(v_j(\beta) - v_i(\beta)) = \operatorname{sgn}\left(\frac{y_j^*}{\overline{y}_j} - \frac{y_i^*}{\overline{y}_i}\right) \text{ for all } i, j \in \mathcal{C}' \text{ and for all } \beta \in (\beta^*, \infty).$$

Hence, if $(\mathcal{C}, \mathcal{R})$ is strongly connected then, by Corollary 4.9 (a), the sum on the right hand side of (4.23) is negative. On the other hand, if $(\mathcal{C}, \mathcal{R})$ is not strongly connected then we have

$$v_{c'}(\beta) = \frac{y_{c'}^*}{\beta y_{c'}^* + \overline{y}_{c'}} < \frac{1}{\beta} = v_{c'+1}(\beta) = \cdots = v_c(\beta) \text{ for all } \beta \in (0, \infty)$$

(note that we have $\beta^* = 0$ in the "not strongly connected" case). Thus, Corollary 4.9 (b) implies that the sum on the right hand side of (4.23) is, again, negative.

Taking also into account that $p(\beta) > 0$ for all $\beta \in (\beta^*, \infty)$, we obtain (4.19). □

From the point of view of our main results, it suffices to have in hand those properties of p, that were established in Corollary 4.10. However, it may be useful in future works to know more about the function p. Therefore, we examine the higher order derivatives of p in the supplementary Section 4.5.

4.3 Proof of the Deficiency-One Theorem: single linkage class

We prove in this section Theorem 4.2 for the single linkage class case. Since the deficiency-zero case was already treated in Section 4.1, we concentrate on the deficiency-one case in this section.

4.3.1 The weakly reversible case

We now prove the single linkage class deficiency-one case of Theorem 4.2 under the extra assumption of the weak reversibility.

Theorem 4.11 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies $\delta = 1$ and $(\mathcal{C}, \mathcal{R})$ is strongly connected. Then*

(a) $E_+ \neq \emptyset$,

(b) if $x^* \in E_+$ *then* $E_+ = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$, *and*

(c) $|E_+ \cap \mathcal{P}| = 1$ *for each positive stoichiometric class* $\mathcal{P}$.

Proof Since $(\mathcal{C}, \mathcal{R})$ is strongly connected, we have $\ell = t = 1$. Thus, by Proposition 2.12, $\dim(\ker B \cap \operatorname{ran}_\kappa I) = 1$ follows from the assumption $\delta = 1$. Let $0 \neq h \in \ker B \cap \operatorname{ran} I_\kappa$. Let $\overline{y} \in \mathbb{R}^c_+$ and $y^* \in \mathbb{R}^c_{\geq 0}$ be such that $I_\kappa \overline{y} = 0, I_\kappa y^* = h$, and at least one coordinate of y^* is 0. The existence of such a $\overline{y}$ and y^* is guaranteed by Lemma 2.5 (see that part of Remark 4.8, which concerns the strongly connected case).

Let $x \in \mathbb{R}^n_+$ and recall that $x \in E_+$ if and only if $I_\kappa \cdot \Theta(x) \in \ker B$. Hence, $x \in E_+$ if and only if $\Theta(x) = \alpha y^* + \gamma \overline{y}$ for some $\alpha, \gamma \in \mathbb{R}$. Note that $\Theta(x) \in \mathbb{R}^c_+$ and note also that $\alpha y^* + \gamma \overline{y} \in \mathbb{R}^c_+$ if and only if $\gamma > 0$ and $\alpha / \gamma > \beta^*$, where

$$\beta^* = \max\{-\overline{y}_i / y_i^* \mid i \in \mathcal{C} \text{ and } y_i^* > 0\}.$$

Taking the logarithm of both sides of $\Theta(x) = \alpha y^* + \gamma \overline{y}$ coordinatewise yields $B^\top \log(x) = \log(\alpha y^* + \gamma \overline{y})$, or equivalently, $\widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = \log\left(\frac{\alpha}{\gamma} y^* + \overline{y}\right)$. Thus, a vector $x \in \mathbb{R}^n_+$ is also in E_+ if and only if there exists a $\beta \in (\beta^*, \infty)$ and there exists a $\gamma \in \mathbb{R}_+$ such that

$$\log(\beta y^* + \overline{y}) = \widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix}.$$

Indeed, once β is fixed, α is given by the formula $\alpha = \beta\gamma$. Therefore, we examine the inclusion $\log(\beta y^* + \overline{y}) \in \operatorname{ran} \widehat{B}^\top$ for $\beta \in (\beta^*, \infty)$.

Since $\ker B \cap \operatorname{ran} I_\kappa = \ker \widehat{B}$, we have $\ker \widehat{B} = \operatorname{span}(h)$ and therefore $\operatorname{ran} \widehat{B}^\top = (\operatorname{span}(h))^\perp$ (see the choice of h). Let us define $g : (\beta^*, \infty) \to \mathbb{R}$ by

$$g(\beta) = \langle h, \log(\beta y^* + \overline{y}) \rangle = \log\left(\prod_{i \in \mathcal{C}} (\beta y_i^* + \overline{y}_i)^{h_i} \right) \quad (\beta \in (\beta^*, \infty)).$$

It is clear that for $\beta \in (\beta^*, \infty)$ we have $\log(\beta y^* + \overline{y}) \in \operatorname{ran} \widehat{B}^\top$ if and only if $g(\beta) = 0$. By Corollary 4.10 (d), the function $\beta \overset{p}{\mapsto} \prod_{i \in \mathcal{C}} (\beta y_i^* + \overline{y}_i)^{h_i}$ is a bijection between (β^*, ∞) and $\mathbb{R}_+$. Hence, there exists a unique $\beta \in (\beta^*, \infty)$ such that $p(\beta) = 1$, and therefore g has a unique root. Since $\log : \mathbb{R}^n_+ \to \mathbb{R}^n$ and $-\log : \mathbb{R}_+ \to \mathbb{R}$ are bijections, we directly obtain that $E_+ \neq \emptyset$. This concludes the proof of (a).

Statements (b) and (c) follow immediately from Corollaries 4.4 and 4.5, respectively. □

We saw in the above proof that both the existence and the uniqueness of the positive steady states relied on the properties of the power function p (beside, of course, Corollary 4.5). It is clear that the existence of a positive steady state is equivalent to the existence of $\beta \in (\beta^*, \infty)$ such that $p(\beta) = 1$. Thus, in respect of the existence of a positive steady state, the crucial properties of the continuous function p are that

$$\lim_{\beta \to \beta^* + 0} p(\beta) = \infty \text{ and}$$
$$\lim_{\beta \to \infty} p(\beta) = 0.$$

Also, it is apparent that the uniqueness of the positive steady state is a consequence of the fact that there is only one $\beta \in (\beta^*, \infty)$ such that $p(\beta) = 1$. Thus, in respect of the uniqueness of the positive steady state, the crucial property of the differentiable function p is that

$$(\partial p)(\beta) < 0 \text{ for all } \beta \in (\beta^*, \infty).$$

At this point we explain the main difference between the proof Feinberg given for the above theorem in [29] and the one we presented here. So assume for this paragraph that the assumptions of Theorem 4.11 hold. Then the linear subspace $\ker(B \cdot I_\kappa)$ of $\mathbb{R}^c$ is two-dimensional. Moreover, the intersection $\ker(B \cdot I_\kappa) \cap \mathbb{R}^c_+$ is a two-dimensional manifold. We chose $\overline{y}$ and y^* in the proof of Theorem 4.11 such that $\overline{y} \in \mathbb{R}^c_+$, $y^* \in \operatorname{bd}(\mathbb{R}^c_+)$, $\overline{y} \in \ker I_\kappa$, $y^* \in \ker(B \cdot I_\kappa)$, and

$$\ker(B \cdot I_\kappa) \cap \mathbb{R}^c_+ = \{\alpha y^* + \gamma \overline{y} \mid \gamma > 0 \text{ and } \alpha > \gamma\beta^*\},$$

where $\beta^* = \max\{-\overline{y}_i/y^*_i \mid i \in \mathcal{C} \text{ and } y^*_i > 0\}$. As a matter of fact, Feinberg's choice in [29, Subsection 6.2] is the same when proving the uniqueness of the positive steady states. As it turns out from our proof above, the same choice is appropriate for the proof of the existence. However, for the proof of the existence, Feinberg chose y^1 and y^2 in [29, Subsection 8.1] such that $y^1 \in \operatorname{bd}(\mathbb{R}^c_+)$, $y^2 \in \operatorname{bd}(\mathbb{R}^c_+)$, $y^1 \in \ker(B \cdot I_\kappa)$, $y^2 \in \ker(B \cdot I_\kappa)$, and

$$\ker(B \cdot I_\kappa) \cap \mathbb{R}^c_+ = \{\lambda_1 y^1 + \lambda_2 y^2 \mid \lambda_1 > 0 \text{ and } \lambda_2 > 0\}.$$

As a side remark we mention here that the system in Theorem 4.11 is so called *complex balanced* if and only if $g(0) = 0$ in the above proof. Or equivalently, $\prod_{i=1}^{c} \overline{y}_i^{h_i} = 1$. For more information on complex balancing, please refer to [26] and [38].

4.3.2 The non weakly reversible case

We have demonstrated by the mass action systems (4.2), (4.3), and (4.4) that the non-emptiness of the set of positive steady states may depend on the rate coefficients for single linkage class deficiency-one mass action systems that are not weakly reversible. The aim of this subsection is to provide an equivalent condition to the non-emptiness of E_+ for these mass action systems.

Denote by $\mathcal{C}'$ the set of those complexes, which are in the terminal strong linkage classes of $(\mathcal{C}, \mathcal{R})$ (we do not make any assumption on ℓ and t in this paragraph). Let $\mathcal{C}'' = \mathcal{C} \setminus \mathcal{C}'$. Let $c' = |\mathcal{C}'|$ and $c'' = |\mathcal{C}''|$. Consider $I_\kappa \in \mathbb{R}^{c \times c}$, $\Theta : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^c_{\geq 0}$, and a vector $v \in \mathbb{R}^c$ in the block forms

$$\begin{aligned} I_\kappa &= \begin{bmatrix} I'_\kappa & * \\ 0 & I''_\kappa \end{bmatrix} \in \mathbb{R}^{(c'+c'') \times (c'+c'')}, \\ \Theta &= \begin{bmatrix} \Theta' \\ \Theta'' \end{bmatrix} : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{c'+c''}_{\geq 0}, \text{ and} \\ v &= \begin{bmatrix} v' \\ v'' \end{bmatrix} \in \mathbb{R}^{c'+c''}, \end{aligned} \tag{4.24}$$

where $I'_\kappa \in \mathbb{R}^{c' \times c'}$, $\Theta' : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{c'}_{\geq 0}$, and $v' \in \mathbb{R}^{c'}$ correspond to the complexes in $\mathcal{C}'$ and $I''_\kappa \in \mathbb{R}^{c'' \times c''}$, $\Theta'' : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{c''}_{\geq 0}$, and $v'' \in \mathbb{R}^{c''}$ correspond to the complexes in $\mathcal{C}''$. Note that, by Lemma 2.5, I''_κ is invertible.

We now provide a condition that every non weakly reversible mass action system with nonempty set of positive steady states must satisfy.

Proposition 4.12 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which is not weakly reversible. Assume that $E_+ \neq \emptyset$. Then*

$$\text{there exists a } v \in \ker B \cap \operatorname{ran} I_\kappa \text{ such that } (I''_\kappa)^{-1} v'' \in \mathbb{R}^{c''}_+. \tag{4.25}$$

Moreover, if $v \in \operatorname{ran} I_\kappa$ is such that $(I''_\kappa)^{-1} v'' \in \mathbb{R}^{c''}_+$ then $v(\mathcal{C}'') < 0$ holds, where $v(\mathcal{C}'')$ is understood in accordance with (1.1).

Proof Fix $x^* \in E_+$. Then $I_\kappa \cdot \Theta(x^*) \in \ker B$. Thus, there exists a $v \in \ker B \cap \operatorname{ran} I_\kappa$ such that $I_\kappa \cdot \Theta(x^*) = v$. By (4.24), we have $(I''_\kappa)^{-1} v'' = \Theta''(x^*)$. Since $\Theta(x^*) \in \mathbb{R}^c_+$, we obtain that $(I''_\kappa)^{-1} v'' \in \mathbb{R}^{c''}_+$. This concludes the proof of (4.25).

Fix now $v \in \operatorname{ran} I_\kappa$ such that $(I''_\kappa)^{-1} v'' \in \mathbb{R}^{c''}_+$ and let $y \in \mathbb{R}^c$ be such that $v = I_\kappa y$. Then $y'' = (I''_\kappa)^{-1} v''$ and therefore $y'' \in \mathbb{R}^{c''}_+$. Let us define $z : \mathcal{R} \to \mathbb{R}_+$ by $z_{(i,j)} = \kappa_{ij} y_i$. Then, by Proposition 2.3, we have

$$v(\mathcal{C}'') = \operatorname{excess}_z(\mathcal{C}'') = z(\varrho^{\mathrm{in}}(\mathcal{C}'')) - z(\varrho^{\mathrm{out}}(\mathcal{C}'')) < 0,$$

where the inequality follows from $\varrho^{\mathrm{in}}(\mathcal{C}'') = \emptyset$, $\varrho^{\mathrm{out}}(\mathcal{C}'') \neq \emptyset$, and $z > 0$. □

We are now in the position to state our main contribution to the Deficiency-One Theorem.

Theorem 4.13 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies $\delta = 1$, $\ell = t = 1$, and $(\mathcal{C}, \mathcal{R})$ is not strongly connected. Let $0 \neq h \in \ker B \cap \operatorname{ran} I_\kappa$ be such that $h(\mathcal{C}'') \leq 0$. Then*

(a) if $h(\mathcal{C}'') = 0$ then $E_+ = \emptyset$,

(b) if $h(\mathcal{C}'') < 0$ then $E_+ \neq \emptyset$ if and only if $(I''_\kappa)^{-1} h'' \in \mathbb{R}^{c''}_+$ (i.e., all the coordinates of $(I''_\kappa)^{-1} h''$ are positive),

(c) if $E_+ \neq \emptyset$ and $x^* \in E_+$ then $E_+ = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$, and

(d) if $E_+ \neq \emptyset$ then $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$.

Remark 4.14 Note that $\operatorname{ran} I = \operatorname{ran} I_\kappa$ and $\dim(\ker B \cap \operatorname{ran} I) = 1$ hold under the assumptions of Theorem 4.13. Thus, if $0 \neq h \in \ker B \cap \operatorname{ran} I_\kappa$ is such that $h(\mathcal{C}'') < 0$ then h is determined up to a positive scalar multiplier. However, this positive scalar multiplier does not affect the condition $(I''_\kappa)^{-1} h'' \in \mathbb{R}^{c''}_+$. □

Remark 4.15 Before the proof of Theorem 4.13, we comment on the meaning of $(I''_\kappa)^{-1}h'' \in \mathbb{R}^{c''}_+$ in the language of graph theory. Let $h \in \operatorname{ran} I_\kappa$. Since I_κ is block upper triangular and I''_κ is invertible, we obtain that if $y^{*,1}, y^{*,2} \in \mathbb{R}^c$ are such that $I_\kappa y^{*,1} = I_\kappa y^{*,2} = h$ then $y^{*,1}_i = y^{*,2}_i$ for all $i \in \mathcal{C}''$. Let $y^* \in \mathbb{R}^c$ be such that $I_\kappa y^* = h$. Define the function $z^* : \mathcal{R} \to \mathbb{R}$ as in Remark 2.4 (i.e., let $z^*(i,j) = \kappa_{ij} y^*_i$ $((i,j) \in \mathcal{R})$). As a consequence, we obtain that the value $z^*(a)$ is uniquely determined for all $i \in \mathcal{C}''$ and for all $a \in \varrho^{\text{out}}(i)$ (provided that κ and h are fixed, while y^* varies such that $I_\kappa y^* = h$ holds). Condition $(I''_\kappa)^{-1}h'' \in \mathbb{R}^{c''}_+$ expresses that all these values are positive. □

Proof of Theorem 4.13 Statement (a) is an immediate consequence of Proposition 4.12.

Assume for the rest of this proof that $h(\mathcal{C}'') < 0$. The necessity of $(I''_\kappa)^{-1}h'' \in \mathbb{R}^{c''}_+$ for the non-emptiness of E_+ follows from Proposition 4.12. To prove the other direction of the equivalence in (b), assume that $(I''_\kappa)^{-1}h'' \in \mathbb{R}^{c''}_+$. Let $\overline{y}, y^* \in \mathbb{R}^c_{\geq 0}$ be such that $I_\kappa \overline{y} = 0$, $I_\kappa y^* = h$,

$$\begin{aligned} &\text{for all } j \in \mathcal{C} \text{ we have } \overline{y}_j > 0 \text{ if and only if } j \in \mathcal{C}', \\ &\text{for all } j \in \mathcal{C}\backslash\mathcal{C}' \text{ we have } y^*_j > 0, \text{ and} \\ &\text{there exists a } j \in \mathcal{C}' \text{ such that } y^*_j = 0. \end{aligned} \tag{4.26}$$

The existence of such a $\overline{y}$ and y^* is guaranteed by Lemma 2.5 and the fact that $(I''_\kappa)^{-1}h'' \in \mathbb{R}^{c''}_+$ (see that part of Remark 4.8, which concerns the non strongly connected case).

From this point on, the proof is similar to the adequate part of the proof of Theorem 4.11.

Let $x \in \mathbb{R}^n_+$. Recall that $x \in E_+$ if and only if $I_\kappa \cdot \Theta(x) \in \ker B$. Hence, $x \in E_+$ if and only if $\Theta(x) = \alpha y^* + \gamma \overline{y}$ for some $\alpha, \gamma \in \mathbb{R}$. Note that $\Theta(x) \in \mathbb{R}^c_+$. Note also that $\alpha y^* + \gamma \overline{y} \in \mathbb{R}^c_+$ if and only if $\alpha, \gamma > 0$ (see (4.26)). Taking the logarithm of both sides of $\Theta(x) = \alpha y^* + \gamma \overline{y}$ coordinatewise yields $B^\top \log(x) = \log(\alpha y^* + \gamma \overline{y})$, or equivalently, $\widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = \log\left(\frac{\alpha}{\gamma} y^* + \overline{y}\right)$. Thus, a vector $x \in \mathbb{R}^n_+$ is also in E_+ if and only if there exists a $\beta \in (0,\infty)$ and there exists a $\gamma \in \mathbb{R}_+$ such that

$$\log(\beta y^* + \overline{y}) = \widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix}.$$

Indeed, once β is fixed, α is given by the formula $\alpha = \beta\gamma$. Therefore, we examine the inclusion $\log(\beta y^* + \overline{y}) \in \operatorname{ran} \widehat{B}^\top$ for $\beta \in (0,\infty)$.

Since $\ker B \cap \operatorname{ran} I_\kappa = \ker \widehat{B}$, we have $\ker \widehat{B} = \operatorname{span}(h)$ and therefore $\operatorname{ran} \widehat{B}^\top = (\operatorname{span}(h))^\perp$ (see the choice of h). Let us define $g : (0,\infty) \to \mathbb{R}$ by

$$g(\beta) = \langle h, \log(\beta y^* + \overline{y}) \rangle = \log\left(\prod_{i \in \mathcal{C}} (\beta y^*_i + \overline{y}_i)^{h_i}\right) \quad (\beta \in (0,\infty)).$$

It is clear that for $\beta \in (0,\infty)$ we have $\log(\beta y^* + \overline{y}) \in \operatorname{ran} \widehat{B}^\top$ if and only if $g(\beta) = 0$. By Corollary 4.10 (d), the function $\beta \overset{p}{\mapsto} \prod_{i \in \mathcal{C}} (\beta y^*_i + \overline{y}_i)^{h_i}$ is a bijection between $(0,\infty)$ and $\mathbb{R}_+$. Hence, there exists a unique $\beta \in (0,\infty)$ such that $p(\beta) = 1$, and therefore g has a unique root.

Since $\log : \mathbb{R}_+^n \to \mathbb{R}^n$ and $-\log : \mathbb{R}_+ \to \mathbb{R}$ are bijections, we directly obtain that $E_+ \neq \emptyset$. This concludes the proof of (a).

Statements (b) and (c) follow immediately from Corollaries 4.4 and 4.5, respectively. $\square$

Similarly as after the proof of Theorem 4.11, we can draw the conclusions that in respect of the existence of a positive steady state, the crucial properties of the continuous function p are that

$$\lim_{\beta \to 0+0} p(\beta) = \infty \text{ and}$$
$$\lim_{\beta \to \infty} p(\beta) = 0,$$

while in respect of the uniqueness of the positive steady state, the crucial property of the differentiable function p is that

$$(\partial p)(\beta) < 0 \text{ for all } \beta \in (0, \infty).$$

We summarise Theorems 4.6, 4.11, and 4.13 in the following theorem.

Theorem 4.16 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system for which $\ell = t = 1$ and $\delta \leq 1$. Then*

(a) if $\delta = 0$ then $E_+ \neq \emptyset$ if and only if $(\mathcal{C}, \mathcal{R})$ is strongly connected,

(b) if $\delta = 1$ and $(\mathcal{C}, \mathcal{R})$ is strongly connected then $E_+ \neq \emptyset$,

(c) if $\delta = 1$ and $(\mathcal{C}, \mathcal{R})$ is not strongly connected then

$$E_+ \neq \emptyset \textit{ if and only if all the coordinates of } (I''_\kappa)^{-1} h'' \textit{ are positive,}$$

where $0 \neq h \in \ker B \cap \operatorname{ran} I_\kappa$ is such that $h(\mathcal{C}'') \leq 0$,

(d) if $E_+ \neq \emptyset$ and $x^* \in E_+$ then $E_+ = \{x \in \mathbb{R}_+^n \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$, and

(e) if $E_+ \neq \emptyset$ then $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$.

Proof Statements (a) and (b) follow from Theorems 4.6 and 4.11, respectively. Statement (c) follows from Theorem 4.13 and Proposition 4.12.

Statement (d) and (e) directly follow from Theorems 4.6, 4.11, and 4.13. $\square$

Theorem 4.16 (c), which was worked out by the author of this thesis, makes the Deficiency-One Theorem complete in respect of the existence of positive steady states.

It is clear that for a mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ that satisfies the assumptions of Theorem 4.16, the non-emptiness of E_+ does not depend on the rate coefficients of those reactions for which both the reactant complex and the product complex lie in the terminal strong linkage class. Also, if $\delta = 1$, $\ell = t = 1$, $(\mathcal{C}, \mathcal{R})$ is not strongly connected, and C_i does not lie in the terminal strong linkage class then the non-emptiness of E_+ does not depend on the separate elements of the set

$$\{\kappa_{ij} \mid j \in \mathcal{C}', (i,j) \in \mathcal{R}\}. \tag{4.27}$$

Rather, it depends on the sum

$$\sum_{\substack{(i,j)\in\mathcal{R}\\ j\in\mathcal{C}'}} \kappa_{ij},$$

because this sum appears in the ith diagonal entry of I''_κ, while the elements of the set (4.27) does not appear separately in I''_κ.

In order to illustrate the result of Theorem 4.13, we conclude this subsection by the analysis of the mass action systems (4.2), (4.3), and (4.4). This analysis is based on Theorem 4.13. These three examples illustrate those three different kind of phenomena that can occur when rate coefficients are assigned to a single linkage class deficiency-one reaction network that is not weakly reversible:

- $E_+ \neq \emptyset$ (regardless of the values of the rate coefficients),
- $E_+ = \emptyset$ (regardless of the values of the rate coefficients), and
- the non-emptiness of E_+ depends on the values of the rate coefficients.

The whole Chapter 6 is devoted to the characterisation of these three cases.

Analysis of the mass action system (4.2) Note that $\ell = t = 1$, $\mathcal{C}' = \{C_1, C_2\}$, $\mathcal{C}'' = \{C_3\}$, $n = 2$, $c = 3$, and $\operatorname{ran} S = \operatorname{span}\left([1,-1]^\top\right)$ (the numbering of the complexes is given implicitly in (4.2) by the indices of the rate coefficients). Therefore $\delta = 3 - 1 - 1 = 1$. Further quantities of the system are

$$\widehat{B} = \begin{bmatrix} 0 & 1 & 2 \\ 2 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix},\ h = \begin{bmatrix} -1 \\ 2 \\ -1 \end{bmatrix},\ h'' = \begin{bmatrix} -1 \end{bmatrix},\ I_\kappa = \begin{bmatrix} -\kappa_{12} & \kappa_{21} & 0 \\ \kappa_{12} & -\kappa_{21} & \kappa_{32} \\ 0 & 0 & -\kappa_{32} \end{bmatrix},$$

$$I''_\kappa = \begin{bmatrix} -\kappa_{32} \end{bmatrix},\ (I''_\kappa)^{-1} = -\frac{1}{\kappa_{32}}\begin{bmatrix} 1 \end{bmatrix},\ \text{and } (I''_\kappa)^{-1}h'' = \frac{1}{\kappa_{32}}\begin{bmatrix} 1 \end{bmatrix}.$$

By Theorem 4.13, we obtain that $E_+ \neq \emptyset$ (regardless of the values of the rate coefficients). Moreover, each positive stoichiometric class contains exactly one positive steady state. □

Analysis of the mass action system (4.3) Note that $\ell = t = 1$, $\mathcal{C}' = \{C_1\}$, $\mathcal{C}'' = \{C_2, C_3\}$, $n = 2$, $c = 3$, and $\operatorname{ran} S = \operatorname{span}\left([1,-1]^\top\right)$ (the numbering of the complexes is given implicitly in (4.3) by the indices of the rate coefficients). Therefore $\delta = 3 - 1 - 1 = 1$. Further quantities of the system are

$$\widehat{B} = \begin{bmatrix} 0 & 1 & 2 \\ 2 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix},\ h = \begin{bmatrix} 1 \\ -2 \\ 1 \end{bmatrix},\ h'' = \begin{bmatrix} -2 \\ 1 \end{bmatrix},\ I_\kappa = \begin{bmatrix} 0 & \kappa_{21} & 0 \\ 0 & -\kappa_{21} & \kappa_{32} \\ 0 & 0 & -\kappa_{32} \end{bmatrix},$$

$$I''_\kappa = \begin{bmatrix} -\kappa_{21} & \kappa_{32} \\ 0 & -\kappa_{32} \end{bmatrix},\ (I''_\kappa)^{-1} = -\frac{1}{\kappa_{21}\kappa_{32}}\begin{bmatrix} \kappa_{32} & \kappa_{32} \\ 0 & \kappa_{21} \end{bmatrix},\ \text{and } (I''_\kappa)^{-1}h'' = \frac{1}{\kappa_{21}\kappa_{32}}\begin{bmatrix} \kappa_{32} \\ -\kappa_{21} \end{bmatrix}.$$

By Theorem 4.13, we obtain that $E_+ = \emptyset$ (regardless of the values of the rate coefficients). $\square$

Analysis of the mass action system (4.4) Note that $\ell = t = 1$, $\mathcal{C}' = \{C_1\}$, $\mathcal{C}'' = \{C_2, C_3\}$, $n = 2$, $c = 3$, and $\operatorname{ran} S = \operatorname{span}\left([1, -1]^\top\right)$ (the numbering of the complexes is given implicitly in (4.4) by the indices of the rate coefficients). Therefore $\delta = 3 - 1 - 1 = 1$. Further quantities of the system are

$$\widehat{B} = \begin{bmatrix} 0 & 1 & 2 \\ 2 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix}, \; h = \begin{bmatrix} 1 \\ -2 \\ 1 \end{bmatrix}, \; h'' = \begin{bmatrix} -2 \\ 1 \end{bmatrix}, \; I_\kappa = \begin{bmatrix} 0 & \kappa_{21} & 0 \\ 0 & -(\kappa_{21} + \kappa_{23}) & \kappa_{32} \\ 0 & \kappa_{23} & -\kappa_{32} \end{bmatrix},$$

$$I''_\kappa = \begin{bmatrix} -(\kappa_{21} + \kappa_{23}) & \kappa_{32} \\ \kappa_{23} & -\kappa_{32} \end{bmatrix}, \; (I''_\kappa)^{-1} = -\frac{1}{\kappa_{21}\kappa_{32}} \begin{bmatrix} \kappa_{32} & \kappa_{32} \\ \kappa_{23} & \kappa_{21} + \kappa_{23} \end{bmatrix}, \text{ and}$$

$$(I''_\kappa)^{-1} h'' = \frac{1}{\kappa_{21}\kappa_{32}} \begin{bmatrix} \kappa_{32} \\ \kappa_{23} - \kappa_{21} \end{bmatrix}.$$

By Theorem 4.13, we obtain that $E_+ \neq \emptyset$ if and only if $\kappa_{23} > \kappa_{21}$. Moreover, if $E_+ \neq \emptyset$ then each positive stoichiometric class contains exactly one positive steady state. $\square$

4.4 Proof of the Deficiency-One Theorem: multiple linkage classes

So far have provided a description of the set of positive steady states for single linkage class mass action systems with $\delta \leq 1$ (which is the Deficiency-One Theorem for the single linkage class case). In this section, we prove the multiple linkage class case of the Deficiency-One Theorem. We will assume that $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$ holds. Since we have already examined such systems in Chapter 3, we now only need to couple the results of Chapter 3 and Sections 4.1 and 4.3.

Theorem 4.17 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system which satisfies*

(i) $\delta^r \leq 1$ for all $r \in \overline{1, \ell}$,

(ii) $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$, and

(iii) $\ell = t$.

Then

(a) $E_+ \neq \emptyset$ if and only if $E_+^r \neq \emptyset$ for all $r \in \overline{1, \ell}$ and

(b) if $E_+ \neq \emptyset$ then

(ba) $x^* \in E_+$ implies that $E_+ = \{x \in \mathbb{R}^n_+ \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}$,

(bb) $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$, and

(bc) E_+ *is* C^∞*-diffeomorphic to* $\mathbb{R}^{n-\operatorname{rank} S}$ *(and hence* E_+ *is connected).*

Proof Statement (a) directly follows from Theorem 3.6. (Only assumption (ii) is crucial in this respect.)

Assume for the rest of this proof that $E_+ \neq \emptyset$. To prove (ba), fix $x^* \in E_+$. By Proposition 3.1, we have $E_+ = \cap_{r=1}^{\ell} E_+^r$. Thus, $x^* \in E_+^r$ for all $r \in \overline{1,\ell}$. Recall that we considered the stoichiometric matrix S in Section 2.7 and Chapter 3 in the block form $S = [S^1, S^2, \ldots, S^\ell]$. Thus, by Theorem 4.16 (d), we obtain that

$$\begin{aligned} E_+ &= \{x \in \mathbb{R}_+^n \mid \log(x) - \log(x^*) \in (\operatorname{ran} S^r)^\perp \text{ for all } r \in \overline{1,\ell}\} = \\ &= \{x \in \mathbb{R}_+^n \mid \log(x) - \log(x^*) \in (\operatorname{ran} S)^\perp\}, \end{aligned}$$

which proves (ba).

Part (bb) and (bc) are direct consequences of Lemma 3.3 (a) and (b), respectively. □

We remark that Theorems 4.16 and 4.17 can easily be adopted to the case of those more general rate functions that were investigated by Sontag in [54]. The rate of the reaction (i,j) at x in [54] is $\kappa_{ij} \prod_{s=1}^n \theta_s(x_s)^{B_{si}}$ for appropriate functions $\theta_1, \ldots, \theta_n : \mathbb{R} \to \mathbb{R}_{\geq 0}$. The special case $\theta_1(y) = \cdots = \theta_n(y) = |y|$ for $y \in \mathbb{R}$ yields (2.6).

We conclude this section by showing two examples and also their analysis for the case $\ell = t = 2$. In (4.28), the first linkage class is not strongly connected and its deficiency is one, the second linkage class is strongly connected and its deficiency is zero, while the whole network is of deficiency-one. In (4.29), both linkage classes are not strongly connected and their deficiencies are one, while the whole network is of deficiency-two.

$$\begin{gathered} 2X_1 \underset{\kappa_{23}}{\overset{\kappa_{32}}{\rightleftarrows}} X_1 + X_2 \xrightarrow{\kappa_{21}} 2X_2 \\ X_1 \underset{\kappa_{45}}{\overset{\kappa_{54}}{\rightleftarrows}} X_3 \end{gathered} \tag{4.28}$$

$$\begin{gathered} 2X_1 \underset{\kappa_{23}}{\overset{\kappa_{32}}{\rightleftarrows}} X_1 + X_2 \xrightarrow{\kappa_{21}} 2X_2 \\ 3X_1 \underset{\kappa_{56}}{\overset{\kappa_{65}}{\rightleftarrows}} 2X_1 + X_3 \xrightarrow{\kappa_{54}} X_1 + 2X_3 \end{gathered} \tag{4.29}$$

The analysis below of the mass action systems (4.28) and (4.29) is based on the results of this chapter.

Analysis of (4.28) Note that $\ell = t = 2$, $(\mathcal{C}^1)' = \{C_1\}$, $(\mathcal{C}^1)'' = \{C_2, C_3\}$, $\mathcal{C}^2 = \{C_4, C_5\}$, $n = 3$, $c^1 = 3$, $c^2 = 2$, $c = 5$, $\operatorname{ran} S^1 = \operatorname{span}([1,-1,0]^\top)$, $\operatorname{ran} S^2 = \operatorname{span}([1,0,-1]^\top)$, and $\operatorname{ran} S = \operatorname{span}([1,-1,0]^\top, [1,0,-1]^\top)$ (the numbering of the complexes is given implicitly in (4.28) by the indices of the rate coefficients). Therefore $\delta^1 = 3 - 1 - 1 = 1$, $\delta^2 = 2 - 1 - 1 = 0$, and $\delta = 5 - 2 - 2 = 1$. Hence, all the assumptions of Theorem 4.17 are satisfied. Therefore, it suffices to check the non-emptiness of the set of positive steady states for the two linkage classes separately. Since the first linkage class is the same as (4.4), we already know that $E_+^1 \neq \emptyset$ if and only if $\kappa_{23} > \kappa_{21}$. Since the $\delta^2 = 0$ and $(\mathcal{C}^2, \mathcal{R}^2)$ is strongly connected, $E_+^2 \neq \emptyset$ (regardless of the values of κ_{45} and κ_{54}). Consequently, $E_+ \neq \emptyset$ if and only if $\kappa_{23} > \kappa_{21}$. Moreover, if $E_+ \neq \emptyset$ then each positive stoichiometric class contains exactly one positive steady state. $\square$

Analysis of (4.29) Note that $\ell = t = 2$, $(\mathcal{C}^1)' = \{C_1\}$, $(\mathcal{C}^1)'' = \{C_2, C_3\}$, $(\mathcal{C}^2)' = \{C_4\}$, $(\mathcal{C}^2)'' = \{C_5, C_6\}$, $n = 3$, $c = 6$, $c^1 = 3$, $c^2 = 3$, $\operatorname{ran} S^1 = \operatorname{span}\left([1,-1,0]^\top\right)$, $\operatorname{ran} S^2 = \operatorname{span}\left([1,0,-1]^\top\right)$, and $\operatorname{ran} S = \operatorname{span}\left([1,-1,0]^\top, [1,0,-1]^\top\right)$ (the numbering of the complexes is given implicitly in (4.29) by the indices of the rate coefficients). Therefore $\delta^1 = 3 - 1 - 1 = 1$, $\delta^2 = 3 - 1 - 1 = 1$, and $\delta = 6 - 2 - 2 = 2$. Hence, all the assumptions of Theorem 4.17 are satisfied. Therefore, it suffices to check the non-emptiness of the set of positive steady states for the two linkage classes separately. Since the first linkage class is the same as (4.4), we already know that $E_+^1 \neq \emptyset$ if and only if $\kappa_{23} > \kappa_{21}$. Note that the second linkage class is similar to (4.4). As a matter of fact, the vector h'' and the matrix I_κ'' of the second linkage class equals to the respective objects of (4.4) (after suitable renumbering of the complexes). Therefore, we obtain that $E_+^2 \neq \emptyset$ if and only if $\kappa_{56} > \kappa_{54}$. Consequently, $E_+ \neq \emptyset$ if and only if $\kappa_{23} > \kappa_{21}$ and $\kappa_{56} > \kappa_{54}$. Moreover, if $E_+ \neq \emptyset$ then each positive stoichiometric class contains exactly one positive steady state. $\square$

4.5 Supplement to Section 4.2

Recall the definition of the power function p from Corollary 4.10. In that Corollary, we have establish some properties of p. Since it may be useful in future works to know more about the function p, we examine in this supplementary section its higher order derivatives. We will apply the results of this section only in Section 5.4, where the convexity of a multivariate function related to p is proven. However, that convexity result is not relevant from the point of view of our main results.

Clearly, p is k times continuously differentiable for all $k \geq 1$. Proposition 4.19 below reveals the sign of the higher order derivatives of p. To prepare for that, for fixed $k \geq 1$, define the function $H_k : (\beta^*, \infty) \to \mathbb{R}$ by

$$H_k(\beta) = \sum_{i \in \mathcal{C}} h_i \left(\frac{y_i^*}{\beta y_i^* + \overline{y}_i} \right)^k \quad (\beta \in (\beta^*, \infty)). \tag{4.30}$$

Note that we obtained at the end of the proof of Corollary 4.10 that

$$\operatorname{sgn} \circ H_1 \equiv -1.$$

Proposition 4.18 *In addition to the assumptions of Corollary 4.10, let $k \geq 1$ and let H_k be as in* (4.30)*. Then*

(a) H_1 is k times continuously differentiable and $\partial^k H_1 = (-1)^k \cdot k! \cdot H_{k+1}$,

(b) $\operatorname{sgn} \circ H_k \equiv -1$*, and*

(c) $\operatorname{sgn} \circ \partial^k H_1 \equiv (-1)^{k+1}$*.*

Proof Statement (a) directly follows from (4.30) by induction.

To prove (b), let $v_i(k, \beta) = \left(\frac{y_i^*}{\beta y_i^* + \overline{y}_i}\right)^k$ $(i \in \overline{1, c}, k \geq 1, \beta \in (\beta^*, \infty))$. A short calculation shows that

$$\operatorname{sgn}(v_j(k, \beta) - v_i(k, \beta)) = \operatorname{sgn}(y_j^*/\overline{y}_j - y_i^*/\overline{y}_i)$$

for all $i, j \in \overline{1, c'}$, for all $k \geq 1$, and for all $\beta \in (\beta^*, \infty)$. Therefore, if $(\mathcal{C}, \mathcal{R})$ is strongly connected then we obtain (b) by Corollary 4.9 (a). On the other hand, if $(\mathcal{C}, \mathcal{R})$ is not strongly connected then we have

$$v_{c'}(k, \beta) = \left(\frac{y_{c'}^*}{\beta y_{c'}^* + \overline{y}_{c'}}\right)^k < \left(\frac{1}{\beta}\right)^k = v_{c'+1}(k, \beta) = \cdots = v_c(k, \beta) \text{ for all } \beta \in (0, \infty)$$

(again, note that we have $\beta^* = 0$ in the "not strongly connected" case). Thus, Corollary 4.9 (b) implies $\operatorname{sgn} \circ H_k \equiv -1$.

Statement (c) is an immediate consequence of (a) and (b). □

Proposition 4.19 *In addition to the assumptions of Corollary 4.10, let $N \geq 1$ and let H_1 be as in* (4.30)*. Then*

(a) p is N times continuously differentiable and

$$\partial^N p = \sum_{k=0}^{N-1} \binom{N-1}{k} \cdot \partial^{N-1-k} p \cdot \partial^k H_1 \text{ and} \tag{4.31}$$

(b) $\operatorname{sgn} \circ \partial^N p \equiv (-1)^N$*.*

Proof We already saw in the proof of Corollary 4.10 that $\partial p = p \cdot H_1$. For $N = 1$, this latter proves (a). For $N \geq 2$, differentiation of both sides $N - 1$ times and the Leibniz rule yield (a).

We prove (b) by induction. It is clear from the definition of p that $\operatorname{sgn} \circ p \equiv 1$. Also, we obtained in Corollary 4.10 (c) that $\operatorname{sgn} \circ \partial p \equiv -1$. Assume now that $N \geq 2$ and $\operatorname{sgn} \circ \partial^k p \equiv (-1)^k$ for all $k \in \overline{0, N-1}$. Then, by the induction hypothesis and Proposition 4.18 (c), we have

$$\operatorname{sgn} \circ \left[\binom{N-1}{k} \cdot \partial^{N-1-k} p \cdot \partial^k H_1\right] \equiv (-1)^{N-1-k} \cdot (-1)^{k+1} = (-1)^N$$

for all $k \in \overline{0, N-1}$. Hence, all the N summands on the right hand side of (4.31) have the same sign as $(-1)^N$, which proves (b). □

Based on Corollary 4.10 and Proposition 4.19 (b) we depicted the function p in Figure 4.1.

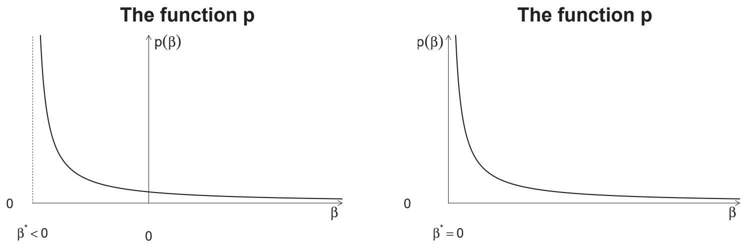
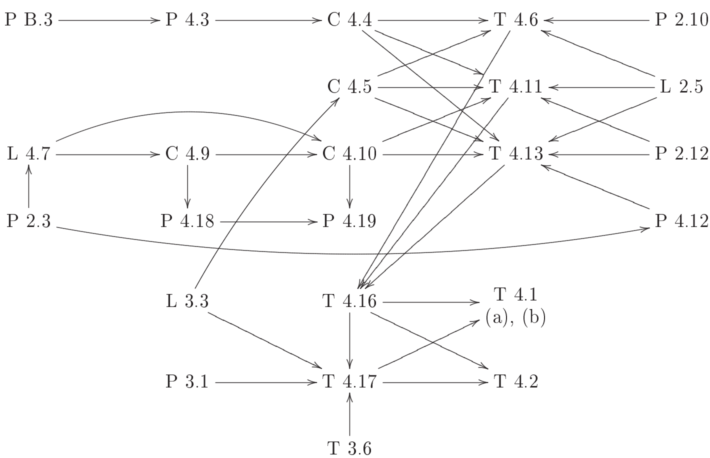


Figure 4.1: The function $p : (\beta^*, \infty) \to \mathbb{R}_+$, which was defined in Corollary 4.10. The strongly connected case is on the left, the non strongly connected case is on the right.

4.6 The acyclic directed graph of the implications

We have depicted below the acyclic directed graph of the implications of this chapter. For the organising principle of this directed graph, see Section 2.8.



Chapter 5

Existence of the positive steady states of weakly reversible deficiency-one mass action systems

We start this chapter by recalling the Deficiency-One Theorem of Feinberg for the weakly reversible case (see Theorem 4.2).

Theorem 5.1 (Deficiency-One Theorem) *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a mass action system, which satisfies*

(i) $\delta^r \leq 1$ *for all* $r \in \overline{1, \ell}$*,*

(ii) $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$*, and*

(iii) $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *is weakly reversible.*

Then $|E_+ \cap \mathcal{P}| = 1$ *for each positive stoichiometric class* $\mathcal{P}$*.*

Consider the eleven reaction networks in Table 5.1. (The symbol "0" appearing in Examples (vi), (vii), (viii), and (ix) in Table 5.1 denote the so called *zero complex*. See [27, Section 4] for more on the zero complex.) Note that all the linkage classes have a deficiency of zero, while the whole network has a deficiency of one for all of these examples. Therefore, the assumption (*ii*) in Theorem 5.1 is not satisfied for these examples. More generally, if

$$\delta^1 = \delta^2 = \cdots = \delta^\ell = 0 \text{ and } \delta = 1$$

then Theorem 5.1 gives no information directly. (In [27, Remark 6.2.B], it is demonstrated on Example (iv) in Table 5.1 that in some cases the Deficiency-One Theorem can still provide information even if the assumptions of the theorem are not satisfied. This justifies the word "directly" at the end of our previous sentence.) This motivates the next theorem, which is the main result of this chapter (and also the main result of [14]).

	Reaction network	Reference(s)
(i)	$X_1 + X_2 \rightleftarrows 2X_3$ $X_1 \rightleftarrows X_2 \rightleftarrows X_3$	[27, (2.13)]
(ii)	$X_1 \rightleftarrows X_2$ $2X_1 \rightleftarrows 2X_2$	[43, (3-21)]
(iii)	$X_1 \rightleftarrows X_2$ $X_3 \rightleftarrows X_4$ $X_1 + X_4 \rightleftarrows X_2 + X_3$	[43, (1-1)]
(iv)	$X_1 \rightleftarrows 2X_1$ $X_1 + X_2 \rightleftarrows X_3 \rightleftarrows X_2$	[27, (6.20)], [28, (3.4)], [29, (2.10)]
(v)	$X_1 \rightleftarrows X_2$ $X_1 + 2X_2 \rightleftarrows 3X_2$	reversible version of [27, (6.24)], [28, (4.24)], [29, (4.11)]; see also [37]
(vi)	$X_1 + X_2 \rightleftarrows 2X_1$ $X_1 \rightleftarrows 0 \rightleftarrows X_2$	[28, (1.1)], [30, (1.1)], [18, Table 1.1 (vi)], [21, Table 1 (vi)]
(vii)	$2X_1 + X_2 \rightleftarrows 3X_1$ $X_1 \rightleftarrows 0 \rightleftarrows X_2$	[28, (1.2)], [30, (1.2)], [18, Table 1.1 (vii)], [21, Table 1 (vii)]
(viii)	$X_1 + 2X_2 \rightleftarrows 3X_1$ $X_1 \rightleftarrows 0 \rightleftarrows X_2$	[18, Table 1.1 (viii)], [21, Table 1 (viii)]
(ix)	$2X_1 + X_2 \rightleftarrows 3X_1$ $0 \rightleftarrows X_1 \rightleftarrows X_2$	[28, (1.3)], [30, (1.3)]
(x)	$X_1 + X_2 \rightleftarrows X_2 + X_3$ $X_1 + X_4 \rightleftarrows X_3 + X_4$	[29, (2.8)]
(xi)	$\begin{array}{ccccccc} X_1 + X_2 & \rightleftarrows & 2X_2 & & X_1 + 3X_5 & \rightarrow & X_2 \\ \uparrow & & \downarrow & & \uparrow & & \downarrow \\ X_3 + X_4 & \rightleftarrows & 2X_4 & & X_1 + X_3 & \leftarrow & X_4 \end{array}$	(2.5)

Table 5.1: Some examples of weakly reversible deficiency-one reaction networks for which each linkage class has a deficiency of zero.

Theorem 5.2 *Let $(\mathcal{X},\mathcal{C},\mathcal{R},\kappa)$ be a mass action system and denote by δ the deficiency of the underlying reaction network $(\mathcal{X},\mathcal{C},\mathcal{R})$. Assume that $(\mathcal{X},\mathcal{C},\mathcal{R})$ is weakly reversible and $\delta = 1$. Then each positive stoichiometric class contains a positive steady state (i.e., $E_+ \cap \mathcal{P} \neq \emptyset$ for each positive stoichiometric class $\mathcal{P}$).*

We emphasise that both the weak reversibility and the fact that the deficiency equals to 1 are properties of the underlying reaction network of a mass action system. Hence, the sufficient condition that guarantees the existence of a positive steady state in each positive stoichiometric class is a property of the underlying reaction network only (i.e., it is not dependent on the precise nature of the kinetics as long as the dynamics follows the mass action law). Qualitative properties that are not dependent on the precise values of the rate coefficients of the mass action system in question could be useful in practice, because these values are often unknown.

The proof of Theorem 5.2 is carried out in Section 5.1, 5.2, and 5.3. We remark that the yet unpublished work [23] by Deng, Feinberg, Jones, and Nachman claims that a generalisation of Theorem 5.2 also holds. Namely, the authors of that manuscript claim that the same implication holds without any assumption on the deficiency of the underlying reaction network. They assume only the weak reversibility of the network, and they claim that this is sufficient to prove the existence of a positive steady state in each positive stoichiometric class. Their proof technique is significantly different from the one presented in this chapter, most of the intermediate results in [23] rely heavily on the weak reversibility of the network, while in our proof of Theorem 5.2 the weak reversibility of the network becomes crucial only in the concluding steps of the proof, namely, after Proposition 5.5 in Section 5.3. Rather, we take advantage of the fact that the deficiency of the network is assumed to be one.

We remark that one cannot expect the conclusion that $|E_+ \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$ in Theorem 5.2 (regardless of the values of the rate coefficients). This is demonstrated by analysing below Example (v) in Table 5.1.

Analysis of Example (v) in Table 5.1 Let the numbering of the complexes in Example (v) in Table 5.1 be $C_1 = X_1, C_2 = X_2, C_3 = X_1 + 2X_2$, and $C_4 = 3X_2$. Accordingly, we have the positive rate coefficients $\kappa_{12}, \kappa_{21}, \kappa_{34}$, and κ_{43}. We demonstrate with this analysis that the choice of the values of the rate coefficients influences the number of positive steady states in the positive stoichiometric classes.

Note that the mass action system in question satisfies the assumptions of Theorem 5.2. Indeed, the underlying reaction network is weakly reversible and the deficiency of the network, δ, equals to 1. This latter fact holds, because the number of complexes, c, equals to 4, the number of linkage classes, ℓ, equals to 2, while the rank of the stoichiometric matrix, $\operatorname{rank} S$, equals to 1. It follows from

$$\operatorname{ran} S = \operatorname{span}\left(\begin{bmatrix} 1 \\ -1 \end{bmatrix}\right)$$

that $\operatorname{rank} S = 1$ indeed holds. The positive stoichiometric classes are the closed line segments that connect $[a, 0]^\top \in \mathbb{R}^2_{\geq 0}$ and $[0, a]^\top \in \mathbb{R}^2_{\geq 0}$ for some $a \in \mathbb{R}_+$. (A few of them are depicted in Figure

5.1.) The differential equation that describes the time evolution of the species concentrations is

$$\begin{bmatrix} \dot{x}_1(\tau) \\ \dot{x}_2(\tau) \end{bmatrix} = \kappa_{12}x_1(\tau)\begin{bmatrix} -1 \\ 1 \end{bmatrix} + \kappa_{21}x_2(\tau)\begin{bmatrix} 1 \\ -1 \end{bmatrix} + \kappa_{34}x_1(\tau)x_2^2(\tau)\begin{bmatrix} -1 \\ 1 \end{bmatrix} + \kappa_{43}x_2^3(\tau)\begin{bmatrix} 1 \\ -1 \end{bmatrix}$$

with state space $\mathbb{R}^2_{\geq 0}$. A short calculation shows that

$$E_+ = \left\{ x = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \in \mathbb{R}^2_+ \;\middle|\; x_1 = x_2 \frac{\kappa_{21} + \kappa_{43}x_2^2}{\kappa_{12} + \kappa_{34}x_2^2} \right\}. \tag{5.1}$$

We depicted the set of positive steady states, E_+, for two different κ's in Figure 5.1.

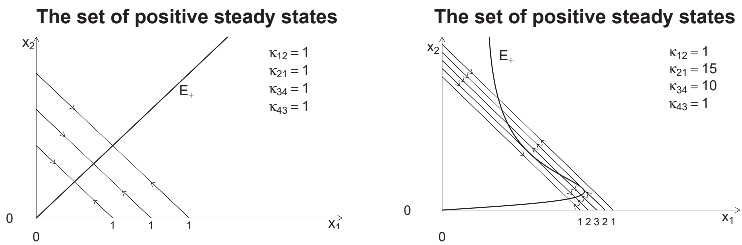


Figure 5.1: The set of positive steady states for Example (v) in Table 5.1 for two different settings of κ. On the left, $\kappa_{12} = 1, \kappa_{21} = 1, \kappa_{34} = 1$, and $\kappa_{43} = 1$, while on the right $\kappa_{12} = 1$, $\kappa_{21} = 15$, $\kappa_{34} = 10$, and $\kappa_{43} = 1$. The numbers under the depicted positive stoichiometric classes indicate the number of positive steady states in the respective positive stoichiometric class.

It is apparent from the right picture on Figure 5.1 (and a short calculation also shows) that in case $\kappa_{12} = 1$, $\kappa_{21} = 15$, $\kappa_{34} = 10$, and $\kappa_{43} = 1$, there exist positive stoichiometric classes $\mathcal{P}_1$, $\mathcal{P}_2$, and $\mathcal{P}_3$ such that $|E_+ \cap \mathcal{P}_1| = 1$, $|E_+ \cap \mathcal{P}_2| = 2$, and $|E_+ \cap \mathcal{P}_3| = 3$. Though stability properties of the steady states are not examined in this thesis, we mention here that $\mathcal{P}_1$ is such that its only positive steady state is globally asymptotically stable relative to $\mathcal{P}_1$. One of the two positive steady states in $\mathcal{P}_2$ is unstable, while the other one is locally asymptotically stable relative to $\mathcal{P}_2$. One of the three positive steady states in $\mathcal{P}_3$ is unstable (the one in the middle), while the other two are locally asymptotically stable relative to $\mathcal{P}_3$.

Finally, we remark that a not so short calculation (which is based on (5.1)) shows that the qualitative picture shown in Figure 5.1 is obtained if and only if the positive numbers κ_{12}, κ_{21}, κ_{34}, and κ_{43} satisfy

$$\frac{\kappa_{43}}{\kappa_{34}} < \frac{\frac{\kappa_{21}}{\kappa_{12}} - 8}{9}.$$

□

We also remark that an algorithm is provided in [28] and [30], which determines whether a *regular* deficiency-one reaction network has the capacity to admit multiple positive steady states. The interested reader should consult [28, Section 2] or [30, Section 2] for the definition of regular reaction networks, however we will not use that concept in this thesis. Here we mention only that a weakly reversible reaction network $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ is regular if and only if

(i) $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ is *reversible* (i.e., if $(i, j) \in \mathcal{R}$ for some $i, j \in \mathcal{C}$ then $(j, i) \in \mathcal{R}$) and

(ii) the undirected graph $(\mathcal{C}, \mathcal{E})$ is a *forest*, where $\mathcal{E} = \{\{i, j\} \subseteq \mathcal{C} \mid \{(i, j), (j, i)\} \cap \mathcal{R} \neq \emptyset\}$.

5.1 Preliminary steps of the proof

The proof of Theorem 5.2 is separated into three main parts. We perform some preliminary steps of the proof in this section. The remaining two main parts of the proof are presented in Sections 5.2 and 5.3, respectively.

Fix until the end of Section 5.3 a mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ and assume that $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ is a weakly reversible deficiency-one chemical reaction network. Unless mentioned otherwise, the symbols

$$n, c, m, \kappa, B, I_\kappa, I, \Theta, R, S, \ell, (\mathcal{C}^r)_{r=1}^{\ell}, (c^r)_{r=1}^{\ell}, (\mathcal{R}^r)_{r=1}^{\ell}, (I_\kappa^r)_{r=1}^{\ell}, L, \delta, \text{ and } \widehat{B}$$

are as defined in Chapter 2. See Tables 2.1 and 2.2 for a summary of these notations.

We provide in this section an equivalent formulation of the fact that $x \in E_+$ (with the help of (5.7) and (5.8) below). By analysing this equivalent condition in Sections 5.2 and 5.3, we will prove that there exists a positive steady state in each positive stoichiometric class. A more detailed outline of the content of Sections 5.2 and 5.3 is provided at the end of this section.

Since the network is weakly reversible and $\delta = 1$, we have $\ker \widehat{B} = \ker B \cap \operatorname{ran} I_\kappa$ and $\dim \ker \widehat{B} = 1$ (see Sections 2.6 and 2.7). Let $0 \neq h \in \ker \widehat{B}$ and consider h in the block form

$$h = \begin{bmatrix} h(1) \\ \vdots \\ h(\ell) \end{bmatrix} \in \mathbb{R}^{\sum_{r=1}^{\ell} c^r},$$

where $h(r) \in \mathbb{R}^{c^r}$ corresponds to the complexes in the rth linkage class ($r \in \overline{1, \ell}$). Since $h \in \operatorname{ran} I$, or equivalently, $h \in \ker L^\top$, we have

$$\sum_{i \in \mathcal{C}^r} h_i = 0 \tag{5.2}$$

for all $r \in \overline{1, \ell}$. Equation (5.2) will be used later on.

We recall Lemma 2.5 for the special case we need in the sequel.

Lemma 5.3 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a weakly reversible mass action system. Denote by ℓ the number of linkage classes and by c^r the number of complexes in the rth linkage class ($r \in \overline{1, \ell}$). Let I_κ be* *as in* (2.8) *and consider* I_κ *in the block-diagonal form*

$$I_\kappa = \begin{bmatrix} I_\kappa^1 & & & 0 \\ & I_\kappa^2 & & \\ & & \ddots & \\ 0 & & & I_\kappa^\ell \end{bmatrix} \in \mathbb{R}^{\left(\sum_{r=1}^{\ell} c^r\right)\times\left(\sum_{r=1}^{\ell} c^r\right)},$$

where I_κ^r *corresponds to the* r*th linkage class* ($r \in \overline{1,\ell}$). *Then* $\dim\ker I_\kappa^r = 1$ *and there exists a* $\overline{y}(r) \in \mathbb{R}_+^{c^r}$ *such that* $\ker I_\kappa^r = \operatorname{span}(\overline{y}(r))$ *for all* $r \in \overline{1,\ell}$.

For $r \in \overline{1,\ell}$ let $\overline{y}(r) \in \mathbb{R}_+^{c^r}$ be such that $I_\kappa^r \cdot \overline{y}(r) = 0$. Clearly, the existence of such a $\overline{y}(r)$ is guaranteed by Lemma 5.3. For $r \in \overline{1,\ell}$ let $y^*(r) \in \operatorname{bd}(\mathbb{R}_+^{c^r})$ be such that $I_\kappa^r \cdot y^*(r) = h(r)$. The existence of such a $y^*(r)$ is guaranteed by Lemma 5.3 and the fact that $h(r) \in \operatorname{ran} I_\kappa^r$. (See Remark 4.8 for a somewhat more detailed explanation on the existence of such a $\overline{y}(r)$ and $y^*(r)$ ($r \in \overline{1,\ell}$).)

Let us define $\overline{y} \in \mathbb{R}^c$ and $y^* \in \mathbb{R}^c$ by the formulas

$$\overline{y} = \begin{bmatrix} \overline{y}(1) \\ \vdots \\ \overline{y}(\ell) \end{bmatrix} \quad \text{and} \quad y^* = \begin{bmatrix} y^*(1) \\ \vdots \\ y^*(\ell) \end{bmatrix},$$

respectively and recall that $\overline{y}(r) \in \mathbb{R}_+^{c^r}$ and $y^*(r) \in \operatorname{bd}(\mathbb{R}_+^{c^r})$ for all $r \in \overline{1,\ell}$.

We claim that

$$y^*(r) = 0 \text{ if and only if } h(r) = 0 \text{ for all } r \in \overline{1,\ell}. \tag{5.3}$$

To prove this claim, fix $r \in \overline{1,\ell}$. Clearly, if $y^*(r) = 0$ then $h(r) = 0$ follows immediately. On the other hand, if $h(r) = 0$ then, by Lemma 5.3, $y^*(r) = \lambda\overline{y}(r)$ for some $\lambda \in \mathbb{R}$. Since $y^*(r) \in \operatorname{bd}(\mathbb{R}_+^{c^r})$ and $\overline{y}(r) \in \mathbb{R}_+^{c^r}$, we obtain that $\lambda = 0$ and $y^*(r) = 0$. The claim (5.3) is therefore proven.

Without loss of generality, we may assume (possibly after reordering the linkage classes) that $\ell' \in \overline{1,\ell}$ is such that

$$\begin{aligned} &y^*(r) \neq 0 \text{ (or equivalently, } h(r) \neq 0) \text{ for all } r \in \overline{1,\ell'} \text{ and} \\ &y^*(r) = 0 \text{ (or equivalently, } h(r) = 0) \text{ for all } r \in \overline{\ell'+1,\ell}. \end{aligned} \tag{5.4}$$

By Propositions 2.11, 2.14, and 2.15, it is easy to see that $\delta = 1$ implies

(i) $\ell' = 1$ if and only if $\delta^1 = 1, \delta^2 = \cdots = \delta^\ell = 0$ and

(ii) $\ell' \geq 2$ if and only if $\delta^1 = \cdots = \delta^\ell = 0$.

Since $\delta = 1$ and $\delta^1 = 1, \delta^2 = \cdots = \delta^\ell = 0$ imply that $\delta = \delta^1 + \delta^2 + \cdots + \delta^\ell$, the case $\ell' = 1$ is already treated by the Deficiency-One Theorem (see Theorem 5.1). Thus, we assume until the end of the proof of Theorem 5.2 (i.e., until the end of Section 5.3) that

$$\ell' \geq 2.$$

In the rest of this section, we analyse the inclusion $x \in E_+$. For this purpose, recall that a vector $x \in \mathbb{R}^n_+$ is in E_+ if and only if $B \cdot I_\kappa \cdot \Theta(x) = 0$. Since $\ker B \cap \operatorname{ran} I_\kappa = \operatorname{span}(h)$, a vector $x \in \mathbb{R}^n_+$ is also in E_+ if and only if there exists an $\alpha \in \mathbb{R}$ such that

$$I_\kappa \cdot \Theta(x) = \alpha h,$$

or equivalently, there exist $\alpha, \gamma_1, \gamma_2, \ldots, \gamma_\ell \in \mathbb{R}$ such that

$$\Theta(x) = \alpha y^* + \begin{bmatrix} \gamma_1 \overline{y}(1) \\ \vdots \\ \gamma_\ell \overline{y}(\ell) \end{bmatrix} \tag{5.5}$$

(see Lemma 5.3 for a description of the kernel of I_κ). Note that $\Theta(x) \in \mathbb{R}^n_+$ for all $x \in \mathbb{R}^n_+$. Because of the sign structure of $\overline{y}$ and y^*, the right hand side of (5.5) is in $\mathbb{R}^n_+$ if and only if $\alpha, \gamma_1, \gamma_2, \ldots, \gamma_\ell \in \mathbb{R}$ satisfy

$$\begin{aligned} &\gamma_r > 0 \text{ for all } r \in \overline{1,\ell} \text{ and} \\ &\frac{\alpha}{\gamma_r} > -\frac{\overline{y}_i}{y_i^*} \text{ for all } r \in \overline{1,\ell'} \text{ and for all } i \in \mathcal{C}^r \text{ such that } y_i^* > 0. \end{aligned}$$

Recall the definition of Θ from Section 2.3. Under the above mentioned conditions on the real numbers $\alpha, \gamma_1, \gamma_2, \ldots, \gamma_\ell$, taking the natural logarithm of both sides of (5.5) yields

$$B^\top \log(x) = \begin{bmatrix} \log(\alpha y^*(1) + \gamma_1 \overline{y}(1)) \\ \vdots \\ \log(\alpha y^*(\ell) + \gamma_\ell \overline{y}(\ell)) \end{bmatrix},$$

or equivalently,

$$\widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma_1) \\ \vdots \\ -\log(\gamma_\ell) \end{bmatrix} = \begin{bmatrix} \log\left(\frac{\alpha}{\gamma_1} y^*(1) + \overline{y}(1)\right) \\ \vdots \\ \log\left(\frac{\alpha}{\gamma_\ell} y^*(\ell) + \overline{y}(\ell)\right) \end{bmatrix}.$$

For $r \in \overline{1,\ell'}$ let

$$\beta_r^* = \max\left\{ -\frac{\overline{y}_i}{y_i^*} \;\middle|\; i \in \mathcal{C}^r \text{ and } y_i^* > 0 \right\}. \tag{5.6}$$

It is clear from the aforementioned facts that an $x \in \mathbb{R}^n_+$ is also in E_+ if and only if there exist $\gamma_1, \gamma_2, \ldots, \gamma_\ell > 0$ and $(\beta_1, \beta_2, \ldots, \beta_{\ell'}) \in \times_{r=1}^{\ell'} (\beta_r^*, \infty)$ such that

$$\widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma_1) \\ \vdots \\ -\log(\gamma_\ell) \end{bmatrix} = \begin{bmatrix} \log(\beta_1 y^*(1) + \overline{y}(1)) \\ \vdots \\ \log(\beta_{\ell'} y^*(\ell') + \overline{y}(\ell')) \\ \log(\overline{y}(\ell'+1)) \\ \vdots \\ \log(\overline{y}(\ell)) \end{bmatrix} \text{ and} \tag{5.7}$$

$$\beta_1 \gamma_1 = \beta_2 \gamma_2 = \cdots = \beta_{\ell'} \gamma_{\ell'}. \tag{5.8}$$

Indeed, if (5.7) and (5.8) holds then (5.5) holds with $\alpha = \beta_1\gamma_1$.

In the rest of the proof of Theorem 5.2, we will make the following main steps. In Section 5.2 we will concentrate on (5.7), while ignoring (5.8). Namely, we will examine the subset of $\times_{r=1}^{\ell'}(\beta_r^*, \infty)$ for which the right hand side of (5.7) is in $\operatorname{ran}\widehat{B}^\top$. Based on this, we introduce three implicit functions (we will denote these by $\mathbf{b}$, $\mathbf{x}$, and $\mathbf{g}$, respectively). The functions $\mathbf{x}$ and $\mathbf{g}$ will depend on the positive stoichiometric class $\mathcal{P}$ in question (thus, we fix $\mathcal{P}$ before the definition of $\mathbf{x}$ and $\mathbf{g}$). These three implicit functions are constructed in such a way that they provide a description of all

$$(\beta_1, \beta_2, \ldots, \beta_{\ell'}) \in \times_{r=1}^{\ell'}(\beta_r^*, \infty), x \in \mathcal{P} \cap \mathbb{R}_+^n, \text{ and } \gamma \in \mathbb{R}_+^\ell$$

such that (5.7) holds. Still in Section 5.2, we prove that $\mathbf{b}$, $\mathbf{x}$, and $\mathbf{g}$ are continuous. In Section 5.3, based on the continuity of $\mathbf{b}$, $\mathbf{x}$, and $\mathbf{g}$ and a multidimensional version of the Bolzano Theorem, we will show the existence of a

$$(\beta_1, \beta_2, \ldots, \beta_{\ell'}) \in \times_{r=1}^{\ell'}(\beta_r^*, \infty), x \in \mathcal{P} \cap \mathbb{R}_+^n, \text{ and } \gamma \in \mathbb{R}_+^\ell$$

such that both (5.7) and (5.8) hold.

5.2 The study of equation (5.7)

In this section, we examine the subset of $\times_{r=1}^{\ell'}(\beta_r^*, \infty)$ for which the right hand side of (5.7) is in $\operatorname{ran}\widehat{B}^\top$.

Since $\ker\widehat{B} = \operatorname{span}(h)$, we have $\operatorname{ran}\widehat{B}^\top = (\operatorname{span}(h))^\perp$. Therefore, the right hand side of (5.7) is in $\operatorname{ran}\widehat{B}^\top$ if and only if

$$\left(\sum_{r=1}^{\ell'}\sum_{i\in\mathcal{C}^r} h_i \log(\beta_r y_i^* + \overline{y}_i)\right) + \left(\sum_{r=\ell'+1}^{\ell}\sum_{i\in\mathcal{C}^r} h_i \log(\overline{y}_i)\right) = 0,$$

or equivalently,

$$\left(\prod_{r=1}^{\ell'}\prod_{i\in\mathcal{C}^r} (\beta_r y_i^* + \overline{y}_i)^{h_i}\right)\left(\prod_{r=\ell'+1}^{\ell}\prod_{i\in\mathcal{C}^r} (\overline{y}_i)^{h_i}\right) = 1.$$

Recall from Section 5.1 that $h(r) = 0$ for all $r \in \overline{\ell'+1, \ell}$. Therefore, $\prod_{i\in\mathcal{C}^r}(\overline{y}_i)^{h_i} = 1$ for all $r \in \overline{\ell'+1, \ell}$. For $r \in \overline{1, \ell'}$, let us define the function $p_r : (\beta_r^*, \infty) \to \mathbb{R}_+$ by

$$p_r(\beta_r) = \prod_{i\in\mathcal{C}^r} (\beta_r y_i^* + \overline{y}_i)^{h_i} \quad (\beta_r \in (\beta_r^*, \infty)). \tag{5.9}$$

With this, we obtain that

$$\text{the right hand side of (5.7) is in } \operatorname{ran}\widehat{B}^\top \text{ if and only if } \textstyle\prod_{r=1}^{\ell'} p_r(\beta_r) = 1. \tag{5.10}$$

As we have already established in Section 4.2, the function p_r is a bijection between (β_r^*, ∞) and $\mathbb{R}_+$ with negative derivative ($r \in \overline{1, \ell'}$).

Recall that we have assumed that $\ell' \geq 2$. We define the function $\mathbf{b} : \times_{r=1}^{\ell'-1}(\beta_r^*, \infty) \to (\beta_{\ell'}^*, \infty)$ by the implicit definition

$$\left(\prod_{r=1}^{\ell'-1} p_r(\beta_r)\right) \cdot p_{\ell'}(\mathbf{b}(\beta)) = 1 \text{ for } \beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty). \tag{5.11}$$

Thus, by (5.10), for $\beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ and $\beta_{\ell'} \in (\beta_{\ell'}^*, \infty)$, the right hand side of (5.7) is in $\operatorname{ran} \widehat{B}^\top$ if and only if $\beta_{\ell'} = \mathbf{b}(\beta)$.

We remark that

$$\mathbf{b}(\beta) = p_{\ell'}^{-1}\left(\frac{1}{p_1(\beta_1)\cdots p_{\ell'-1}(\beta_{\ell'-1})}\right) \text{ for all } \beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty), \tag{5.12}$$

where $p_{\ell'}^{-1} : \mathbb{R}_+ \to (\beta_{\ell'}^*, \infty)$ is the inverse of the bijection $p_{\ell'} : (\beta_{\ell'}^*, \infty) \to \mathbb{R}_+$. Formula (5.12) makes it possible to define the function $\mathbf{b}$ in a somewhat less transparent, but explicit way. Based on Corollary 4.10, we obtain that

$$\lim_0 p_{\ell'}^{-1} = \infty \text{ and} \tag{5.13}$$

$$\lim_\infty p_{\ell'}^{-1} = \beta_{\ell'}^*. \tag{5.14}$$

From this point on, fix $q \in \mathbb{R}_+^n$. Thus, the positive stoichiometric class $\mathcal{P} = (q + \operatorname{ran} S) \cap \mathbb{R}_{\geq 0}^n$ is also fixed. Based on Corollary 4.5 in Chapter 4, we define the functions $\mathbf{x} : \times_{r=1}^{\ell'-1}(\beta_r^*, \infty) \to \mathbb{R}_+^n$ and $\mathbf{g} : \times_{r=1}^{\ell'-1}(\beta_r^*, \infty) \to \mathbb{R}_+^\ell$ by the implicit definition

$$\mathbf{x}(\beta) \in (q + \operatorname{ran} S) \cap \mathbb{R}_+^n \text{ and} \tag{5.15}$$

$$\widehat{B}^\top \begin{bmatrix} \log(\mathbf{x}(\beta)) \\ -\log(\mathbf{g}(\beta)) \end{bmatrix} = \begin{bmatrix} \log(\beta_1 y^*(1) + \overline{y}(1)) \\ \vdots \\ \log(\beta_{\ell'-1} y^*(\ell'-1) + \overline{y}(\ell'-1)) \\ \log(\mathbf{b}(\beta) y^*(\ell') + \overline{y}(\ell')) \\ \log(\overline{y}(\ell'+1)) \\ \vdots \\ \log(\overline{y}(\ell)) \end{bmatrix} \tag{5.16}$$

for $\beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$. Our aim is to show that there exists a $\beta = (\beta_1, \ldots, \beta_{\ell'-1})$ in $\times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ such that

$$\beta_1 \mathbf{g}_1(\beta) = \beta_2 \mathbf{g}_2(\beta) = \cdots = \beta_{\ell'-1} \mathbf{g}_{\ell'-1}(\beta) = \mathbf{b}(\beta) \mathbf{g}_{\ell'}(\beta). \tag{5.17}$$

If this latter satisfied then $\mathbf{x}(\beta) \in E_+ \cap \mathcal{P}$ follows (recall (5.7) and (5.8)).

We show in the rest of this section that the functions $\mathbf{b}, \mathbf{x}$, and $\mathbf{g}$ are continuous. Based on this continuity result, we conclude the proof of Theorem 5.2 in Section 5.3.

Proposition 5.4 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a weakly reversible deficiency-one mass action system with ℓ linkage classes. Let $\mathcal{C}^r$ denote the set of complexes in the rth linkage class, let $c^r = |\mathcal{C}^r|$ ($r \in \overline{1, \ell}$),* *let* $c = |\mathcal{C}|$*, and let* $n = |\mathcal{X}|$*. Let* S *be the stoichiometric matrix and let* $q \in \mathbb{R}^n_+$*. Let* I_κ *be as in* (2.8)*. Let* $\overline{y} \in \mathbb{R}_+^{\sum_{r=1}^{\ell} c^r}$, $y^* \in \mathrm{bd}(\mathbb{R}_+^{\sum_{r=1}^{\ell} c^r})$*, and* $h \in \mathbb{R}^c \backslash \{0\}$ *be such that* $y^*(r) \in \mathrm{bd}(\mathbb{R}^{c^r}_+)$ *for all* $r \in \overline{1,\ell}$*,* $I_\kappa \overline{y} = 0$*, and* $I_\kappa y^* = h$ *hold. Let* ℓ' *be as in* (5.4)*. Let* β^*_r *be as in* (5.6) *and* p_r *be as in* (5.9) $(r \in \overline{1,\ell'})$*. Let*

$$\mathbf{b} : \times_{r=1}^{\ell'-1} (\beta^*_r, \infty) \to (\beta^*_{\ell'}, \infty)$$

be as in (5.11)*. Also, let*

$$\mathbf{x} : \times_{r=1}^{\ell'-1} (\beta^*_r, \infty) \to \mathbb{R}^n_+ \text{ and } \mathbf{g} : \times_{r=1}^{\ell'-1} (\beta^*_r, \infty) \to \mathbb{R}^\ell_+$$

be as in (5.15) *and* (5.16)*. Then* $\mathbf{b}, \mathbf{x}$*, and* $\mathbf{g}$ *are continuous.*

Proof Let us define the function $G : \left(\times_{r=1}^{\ell'-1} (\beta^*_r, \infty)\right) \times \left((\beta^*_{\ell'}, \infty) \times \mathbb{R}^n_+ \times \mathbb{R}^\ell_+\right) \to \mathbb{R}^{c+(n-\mathrm{rank}\, S)}$ by

$$G(\beta, \beta_{\ell'}, x, \gamma) = \left(\begin{array}{c} \widehat{B}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} - \begin{bmatrix} \log(\beta_1 y^*(1) + \overline{y}(1)) \\ \vdots \\ \log(\beta_{\ell'} y^*(\ell') + \overline{y}(\ell')) \\ \log(\overline{y}(\ell'+1)) \\ \vdots \\ \log(\overline{y}(\ell)) \end{bmatrix} \\ V^\top (x - q) \end{array} \right)$$

for $(\beta, \beta_{\ell'}, x, \gamma) \in \left(\times_{r=1}^{\ell'-1} (\beta^*_r, \infty)\right) \times \left((\beta^*_{\ell'}, \infty) \times \mathbb{R}^n_+ \times \mathbb{R}^\ell_+\right)$, where $V \in \mathbb{R}^{n \times (n - \mathrm{rank}\, S)}$ is a matrix, whose columns form a basis in $(\mathrm{ran}\, S)^\perp$. First note that $1 + n + \ell = c + (n - \mathrm{rank}\, S)$ holds, because we assumed that the deficiency equals to 1 (see Definition 2.9). We will apply the Implicit Function Theorem to G (see Theorem C.1 in Appendix C.1). Clearly, the implicit functions are $\mathbf{b}, \mathbf{x}$, and $\mathbf{g}$, so once we have checked the assumptions of the Implicit Function Theorem, we can draw the conclusion that $\mathbf{b}, \mathbf{x}$, and $\mathbf{g}$ are continuous (even more on their smoothness follows, but it is sufficient for our purposes to know that they are continuous).

Clearly, G is continuously differentiable. We will prove that the partial derivative $\partial_{(\beta_{\ell'}, x, \gamma)} G$ of G is nonsingular everywhere on $\left(\times_{r=1}^{\ell'-1} (\beta^*_r, \infty)\right) \times \left((\beta^*_{\ell'}, \infty) \times \mathbb{R}^n_+ \times \mathbb{R}^\ell_+\right)$. Fix $(\beta, \beta_{\ell'}, x, \gamma) \in \left(\times_{r=1}^{\ell'-1} (\beta^*_r, \infty)\right) \times \left((\beta^*_{\ell'}, \infty) \times \mathbb{R}^n_+ \times \mathbb{R}^\ell_+\right)$ and let $v \in \mathbb{R}^{c+(n-\mathrm{rank}\, S)}$ be a vector from the left kernel of $(\partial_{(\beta_{\ell'}, x, \gamma)} G)(\beta, \beta_{\ell'}, x, \gamma)$. Our aim is to show that $v = 0$.

Note that

$$(\partial_\gamma G)(\beta, \beta_{\ell'}, x, \gamma) = \begin{bmatrix} -L \cdot \mathrm{diag}\left(\frac{1}{\gamma_1}, \ldots, \frac{1}{\gamma_\ell}\right) \\ 0_{(n-\mathrm{rank}\, S) \times \ell} \end{bmatrix} \in \mathbb{R}^{(c+(n-\mathrm{rank}\, S)) \times \ell},$$

where $L \in \{0,1\}^{c \times \ell}$ was defined by (2.15), $\mathrm{diag}(1/\gamma_1, \ldots, 1/\gamma_\ell)$ is the diagonal matrix with diagonal entries $1/\gamma_1, \ldots, 1/\gamma_\ell$, while $0_{(n-\mathrm{rank}\, S) \times \ell}$ is the $(n - \mathrm{rank}\, S) \times \ell$ zero matrix. Consider v in the block form $v = \begin{bmatrix} v^1 \\ v^2 \end{bmatrix} \in \mathbb{R}^{c+(n-\mathrm{rank}\, S)}$ with $v^1 \in \mathbb{R}^c$ and $v^2 \in \mathbb{R}^{n-\mathrm{rank}\, S}$. Since $v^\top \cdot$

$(\partial_\gamma G)(\beta, \beta_{\ell'}, x, \gamma) = 0$ and $\mathrm{diag}(1/\gamma_1, \ldots, 1/\gamma_\ell)$ is nonsingular, it follows that $(v^1)^\top L = 0$, i.e., $v^1 \in \operatorname{ran} I$ (recall Proposition 2.7).

Note that

$$(\partial_x G)(\beta, \beta_{\ell'}, x, \gamma) = \begin{bmatrix} B^\top \cdot \mathrm{diag}\left(\frac{1}{x_1}, \ldots, \frac{1}{x_n}\right) \\ V^\top \end{bmatrix} \in \mathbb{R}^{(c+(n-\operatorname{rank} S))\times n},$$

where $\mathrm{diag}(1/x_1, \ldots, 1/x_n)$ is the diagonal matrix with diagonal entries $1/x_1, \ldots, 1/x_n$. Then we obtain that

$$(v^1)^\top \cdot B^\top \cdot \mathrm{diag}(1/x_1, \ldots, 1/x_n) + (v^2)^\top \cdot V^\top = 0. \tag{5.18}$$

We claim that

$$(5.18) \text{ implies } v^2 = 0. \tag{5.19}$$

Indeed, since $v^1 \in \operatorname{ran} I$ and $S = B \cdot I$, we obtain that $Bv^1 \in \operatorname{ran} S$. Also, since the columns of V form a basis in $(\operatorname{ran} S)^\perp$, $Vv^2 \in (\operatorname{ran} S)^\perp$. Denote by T the symmetric and positive definite matrix $\mathrm{diag}(1/x_1, \ldots, 1/x_n)$. Then (5.18) can be written equivalently as $Tu^1 + u^2 = 0$, where $u^1 = Bv^1 \in \operatorname{ran} S$ and $u^2 = Vv^2 \in (\operatorname{ran} S)^\perp$. Therefore,

$$0 = \langle u^1, u^2 \rangle = -\langle u^1, Tu^1 \rangle.$$

Since T is positive definite, we obtain that $u^1 = 0$ and therefore $u^2 = -Tu^1 = 0$. Since $Vv^2 = 0$ and the columns of V are linearly independent, we obtain that $v^2 = 0$, which proves claim (5.19). Also, we have that $Bv^1 = 0$. Since we obtained earlier in this proof that $v^1 \in \ker L^\top$, it follows that $v^1 \in \ker \widehat{B}$ (recall the definition of $\widehat{B}$ from Section 2.7). So $v^1 = \lambda h$ for some $\lambda \in \mathbb{R}$ (see the definition of h at the beginning of Section 5.1).

To prove that $v = 0$, it remains to show that $\lambda = 0$. Note that

$$(\partial_{\beta_{\ell'}} G)_i(\beta, \beta_{\ell'}, x, \gamma) = \begin{cases} \frac{y_i^*}{\beta_{\ell'} y_i^* + \overline{y}_i}, & \text{if } i \in \mathcal{C}^{\ell'}, \\ 0, & \text{if } i \in \mathcal{C} \backslash \mathcal{C}^{\ell'}. \end{cases}$$

Therefore,

$$\langle (\partial_{\beta_{\ell'}} G)(\beta, \beta_{\ell'}, x, \gamma), v \rangle = \lambda \sum_{i \in \mathcal{C}^{\ell'}} h_i \frac{y_i^*}{\beta_{\ell'} y_i^* + \overline{y}_i} = \lambda \frac{(\partial p_{\ell'})(\beta_{\ell'})}{p_{\ell'}(\beta_{\ell'})},$$

where the last equality follows from (4.23). From (4.19) we obtain that $\lambda = 0$. This concludes the proof of the fact that $\partial_{(\beta_{\ell'}, x, \gamma)} G$ is nonsingular on $\left(\times_{r=1}^{\ell'-1} (\beta_r^*, \infty)\right) \times \left((\beta_{\ell'}^*, \infty) \times \mathbb{R}_+^n \times \mathbb{R}_+^\ell\right)$.

Thus, the Implicit Function Theorem is applicable and we are done. $\square$

5.3 The study of both (5.7) and (5.8)

In Section 5.2, we defined the functions $\mathbf{b} : \times_{r=1}^{\ell'-1} (\beta_r^*, \infty) \to (\beta_{\ell'}^*, \infty), \mathbf{x} : \times_{r=1}^{\ell'-1} (\beta_r^*, \infty) \to \mathbb{R}_+^n$, and $\mathbf{g} : \times_{r=1}^{\ell'-1} (\beta_r^*, \infty) \to \mathbb{R}_+^\ell$. Also, we showed that these three functions are continuous, which will play a role in this section. It remains to show that there exists a $\beta = (\beta_1, \dots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ such that (5.17) holds (recall that this is equivalent to $E_+ \cap \mathcal{P} \neq \emptyset$, where $\mathcal{P} = (q + \operatorname{ran} S) \cap \mathbb{R}^n_{\geq 0}$ is the positive stoichiometric class, which was fixed before we defined the functions $\mathbf{x}$ and $\mathbf{g}$ in Section 5.2). Since $\mathbf{g}_r(\beta) > 0$ for all $r \in \overline{1,\ell'}$ and for all $\beta \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$, we obtain that if (5.17) holds then

$$\operatorname{sgn}(\beta_1) = \cdots = \operatorname{sgn}(\beta_{\ell'-1}) = \operatorname{sgn}(\mathbf{b}(\beta)). \tag{5.20}$$

This motivates the examination of the pre-images of the sets $(-\infty, 0)$, $\{0\}$, and $(0, \infty)$ under $\mathbf{b}$. We reveal some properties of $\mathbf{b}$ in the next proposition.

Proposition 5.5 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a weakly reversible deficiency-one mass action system with ℓ linkage classes. Let $\mathcal{C}^r$ denote the set of complexes in the rth linkage class, let $c^r = |\mathcal{C}^r|$ $(r \in \overline{1,\ell})$, and let $c = |\mathcal{C}|$. Let I_κ be as in (2.8). Let $\overline{y} \in \mathbb{R}_+^{\sum_{r=1}^{\ell} c^r}$, $y^* \in \operatorname{bd}(\mathbb{R}_+^{\sum_{r=1}^{\ell} c^r})$, and $h \in \mathbb{R}^c \backslash \{0\}$ be such that $y^*(r) \in \operatorname{bd}(\mathbb{R}_+^{c^r})$ for all $r \in \overline{1,\ell}$, $I_\kappa \overline{y} = 0$, and $I_\kappa y^* = h$ hold. Let ℓ' be as in (5.4). Let β_r^* be as in (5.6) and p_r be as in (5.9) $(r \in \overline{1,\ell'})$. Let*

$$\mathbf{b} : \times_{r=1}^{\ell'-1}(\beta_r^*, \infty) \to (\beta_{\ell'}^*, \infty)$$

be as in (5.11). Let $\beta' \in \times_{r=1}^{\ell'-1}[\beta_r^*, \infty)$ be such that there exists an $r' \in \overline{1, \ell'-1}$ for which $\beta'_{r'} = \beta^*_{r'}$. Also, let $\varepsilon > 0$ and $\beta'' \in \times_{r=1}^{\ell'-1}[\beta_r^* + \varepsilon, \infty]$ be such that there exists an $r'' \in \overline{1, \ell'-1}$ for which $\beta''_{r''} = \infty$. Then

(a) $\lim_{\beta'} \mathbf{b} = \infty$,

(b) $\lim_{\beta''} \mathbf{b} = \beta_{\ell'}^*$,

(c) $(\partial_r \mathbf{b})(\beta) < 0$ *for all* $r \in \overline{1, \ell'-1}$ *and for all* $\beta \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$, *and*

(d) $(\partial^2 \mathbf{b})(\beta) \in \mathbb{R}^{(\ell'-1)\times(\ell'-1)}$ *is positive definite for all* $\beta \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ *(and hence,* $\mathbf{b}$ *is convex).*

Proof Recall (5.12). Obviously, (4.17) and (5.13) yield (a). Similarly, (4.18), (5.14), and the fact that p_r is bounded on $[\beta_r^* + \varepsilon, \infty)$ for all $r \in \overline{1, \ell'-1}$ yield (b).

Based on (5.12), for $r \in \overline{1, \ell'-1}$ and $\beta = (\beta_1, \dots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$, we have

$$(\partial_r \mathbf{b})(\beta) = -\frac{1}{(\partial p_{\ell'})(\mathbf{b}(\beta))} \cdot \frac{(\partial p_r)(\beta_r)}{p_r(\beta_r) \prod_{\widetilde{r}=1}^{\ell'-1} p_{\widetilde{r}}(\beta_{\widetilde{r}})} = -\frac{(\partial p_r)(\beta_r)}{p_r(\beta_r)} \cdot \frac{p_{\ell'}(\mathbf{b}(\beta))}{(\partial p_{\ell'})(\mathbf{b}(\beta))},$$

where we used that $\left(\prod_{\widetilde{r}=1}^{\ell'-1} p_{\widetilde{r}}(\beta_{\widetilde{r}})\right) \cdot p_{\ell'}(\mathbf{b}(\beta)) = 1$. Since ∂p_r is negative on (β_r^*, ∞) for all $r \in \overline{1,\ell'}$ (recall (4.19)), we obtain (c).

Since we do not make use of (d) in the proof of Theorem 5.2, we placed its proof to Section 5.4. □

Based on Proposition 5.5, we depicted schematically the pre-images of the sets $(-\infty, 0)$, $\{0\}$, and $(0, \infty)$ under $\mathbf{b}$ for the case $\ell' - 1 = 2$ in Figure 5.2. The three pictures refer to the cases

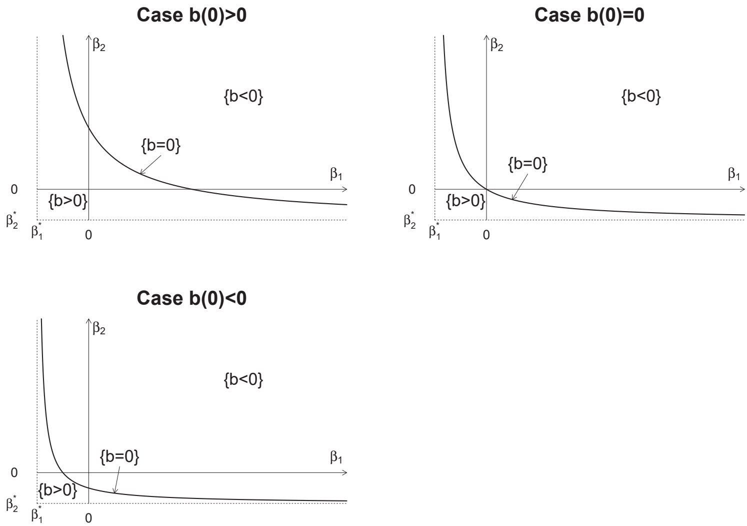


Figure 5.2: The pre-images of the sets $(-\infty, 0)$, $\{0\}$, and $(0, \infty)$ under $\mathbf{b}$ for the case $\ell' - 1 = 2$.

$\mathbf{b}(\mathbf{0}) > 0, \mathbf{b}(\mathbf{0}) = 0$, and $\mathbf{b}(\mathbf{0}) < 0$, respectively, where $\mathbf{0}$ denotes the vector $(0, 0, \ldots, 0) \in \mathbb{R}^{\ell'-1}$. It will become clear why did we depict these three cases separately.

Clearly, if $\mathbf{b}(\mathbf{0}) = 0$ then $\mathbf{0} \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ is the only point, where (5.20) holds. Since (5.17) holds for $\beta = \mathbf{0}$, we directly obtain the existence of a positive steady state. Moreover, the uniqueness also follows immediately (we have $E_+ \cap \mathcal{P} = \{\mathbf{x}(\mathbf{0})\}$). As a side remark, we mention here that the system is called *complex balanced* if $\mathbf{b}(\mathbf{0}) = 0$, or equivalently,

$$\prod_{r=1}^{\ell'} \prod_{i \in \mathcal{C}^r} (\overline{y}_i)^{h_i} = 1.$$

For more on complex balancing, please refer to [26] and [38].

Using (5.11) and that $p_{\ell'}$ is strictly decreasing (see (4.19)), we have

$$\mathbf{b}(\mathbf{0}) < 0 \text{ if and only if } \prod_{r=1}^{\ell'} \prod_{i \in \mathcal{C}^r} (\overline{y}_i)^{h_i} < 1 \text{ and}$$

$$\mathbf{b}(\mathbf{0}) > 0 \text{ if and only if } \prod_{r=1}^{\ell'} \prod_{i \in \mathcal{C}^r} (\overline{y}_i)^{h_i} > 1.$$

Therefore, the cases $\mathbf{b}(\mathbf{0}) < 0$ and $\mathbf{b}(\mathbf{0}) > 0$ are not essentially distinct. Whether one faces $\mathbf{b}(\mathbf{0}) < 0$ or $\mathbf{b}(\mathbf{0}) > 0$ depends on the choice of h at the beginning of Section 5.1. Indeed, one can switch between the two cases by changing h to $-h$ at the beginning of Section 5.1. Therefore, it suffices to treat only one of the two cases in the rest of this proof, say, the case $\mathbf{b}(\mathbf{0}) > 0$. So assume for the rest of this proof that $\mathbf{b}(\mathbf{0}) > 0$.

Clearly, the subset of $\times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$, where (5.20) holds is the (open) set $\mathbb{R}_+^{\ell'-1} \cap \{\mathbf{b} > 0\}$. Denote this latter set by D. Therefore, to find a $\beta \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$ such that (5.17) holds, one needs to search in D. However, for technical reasons a search is made in a strictly larger set. For this purpose, for fixed $r \in \overline{1, \ell'-1}$ define $\beta_r^{**} \in (\beta_r^*, \infty)$ by the implicit definition

$$\left(\prod_{r' \in \overline{1,\ell'} \setminus \{r\}} p_{r'}(0) \right) \cdot p_r(\beta_r^{**}) = 1,$$

or equivalently, by the explicit definition

$$\beta_r^{**} = p_r^{-1} \left(\frac{1}{\prod_{r' \in \overline{1,\ell'} \setminus \{r\}} p_{r'}(0)} \right).$$

Since, $p_r : (\beta_r^*, \infty) \to \mathbb{R}_+$ is a strictly decreasing bijection and $\mathbf{b}(\mathbf{0}) > 0$, β_r^{**} is a uniquely defined positive number. Denote by $\widetilde{D}$ the closed cube $\times_{r=1}^{\ell'-1}[0, \beta_r^{**}]$. Taking into account Proposition 5.5 (c), we have $D \subsetneq \widetilde{D}$. We depicted schematically the sets D and $\widetilde{D}$ for the case $\ell' - 1 = 2$ in Figure 5.3.

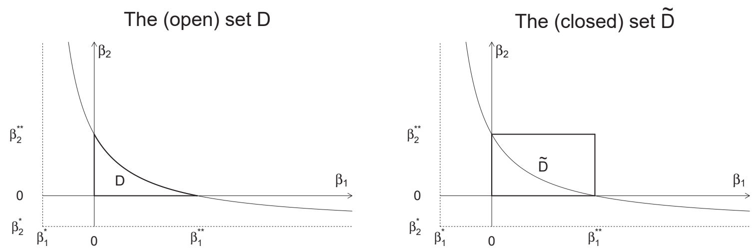


Figure 5.3: The sets $D = \mathbb{R}_+^{\ell'-1} \cap \{\mathbf{b} > 0\}$ and $\widetilde{D} = \times_{r=1}^{\ell'-1}[0, \beta_r^{**}]$ for the case $\ell' - 1 = 2$.

Recall (5.17) and define the function $F : \widetilde{D} \to \mathbb{R}^{\ell'-1}$ by

$$F(\beta) = \begin{pmatrix} \mathbf{b}(\beta)\mathbf{g}_{\ell'}(\beta) \\ \mathbf{b}(\beta)\mathbf{g}_{\ell'}(\beta) \\ \vdots \\ \mathbf{b}(\beta)\mathbf{g}_{\ell'}(\beta) \end{pmatrix} - \begin{pmatrix} \beta_1 \mathbf{g}_1(\beta) \\ \beta_2 \mathbf{g}_2(\beta) \\ \vdots \\ \beta_{\ell'-1}\mathbf{g}_{\ell'-1}(\beta) \end{pmatrix} \quad (\beta = (\beta_1, \beta_2, \ldots, \beta_{\ell'-1}) \in \widetilde{D}).$$

Clearly, to finish the proof of Theorem 5.2, it suffices to show that there exists a $\beta \in \widetilde{D}$ such that $F(\beta) = \mathbf{0}$. As a matter of fact, we already know that such a β must lie in D. However, it is more convenient to have $\widetilde{D}$ as the domain of F, because we can then apply Theorem C.5, which is a multidimensional version of the Bolzano Theorem (for more on the Bolzano Theorem, please refer to Appendix C.2). The continuity of F directly follows from Proposition 5.4. Therefore, to apply Theorem C.5, it is left to check the remaining conditions of Theorem C.5. For this purpose, let $\beta \in \mathrm{bd}(\widetilde{D})$ and let $r \in \overline{1, \ell' - 1}$. On the one hand, if $\beta_r = 0$ then β is in the closure of D. Thus $\mathbf{b}(\beta) \geq 0$, and therefore

$$F_r(\beta) = \mathbf{b}(\beta)\mathbf{g}_{\ell'}(\beta) \geq 0$$

follows. On the other hand, if $\beta_r = \beta_r^{**}$ then $\beta \in \widetilde{D} \backslash D$. Thus $\mathbf{b}(\beta) \leq 0$, and therefore

$$F_r(\beta) = \mathbf{b}(\beta)\mathbf{g}_{\ell'}(\beta) - \beta_r^{**}\mathbf{g}_r(\beta) < 0$$

follows. (We also used in the above arguments that all the coordinate functions of $\mathbf{g}$ are positive functions.) Hence, Theorem C.5 is applicable and it concludes the proof of Theorem 5.2.

5.4 Proof of Proposition 5.5 (d)

Since Proposition 5.5 (d) did not play any role in the proof of Theorem 5.2, we have postponed its proof to this section.

Proof of Proposition 5.5 (d) As we saw in the proof of Proposition 5.5 (c),

$$(\partial \mathbf{b})(\beta) = -\frac{p_{\ell'}}{\partial p_{\ell'}}(\mathbf{b}(\beta)) \cdot \left[\frac{\partial p_1}{p_1}(\beta_1), \ldots, \frac{\partial p_{\ell'-1}}{p_{\ell'-1}}(\beta_{\ell'-1})\right]$$

for all $\beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$. Differentiation of this product yields

$$\begin{aligned}(\partial^2 \mathbf{b})(\beta) =& \frac{p_{\ell'}((\partial p_{\ell'})^2 - p_{\ell'} \cdot \partial^2 p_{\ell'})}{(\partial p_{\ell'})^3}(\mathbf{b}(\beta)) \cdot \begin{bmatrix} \frac{\partial p_1}{p_1}(\beta_1) \\ \vdots \\ \frac{\partial p_{\ell'-1}}{p_{\ell'-1}}(\beta_{\ell'-1}) \end{bmatrix} \cdot \left[\frac{\partial p_1}{p_1}(\beta_1), \ldots, \frac{\partial p_{\ell'-1}}{p_{\ell'-1}}(\beta_{\ell'-1})\right] + \\ &+ \frac{p_{\ell'}}{\partial p_{\ell'}}(\mathbf{b}(\beta)) \cdot \begin{bmatrix} \frac{(\partial p_1)^2 - p_1 \cdot \partial^2 p_1}{p_1^2}(\beta_1) & & 0 \\ & \ddots & \\ 0 & & \frac{(\partial p_{\ell'-1})^2 - p_{\ell'-1} \cdot \partial^2 p_{\ell'-1}}{p_{\ell'-1}^2}(\beta_{\ell'-1}) \end{bmatrix}\end{aligned} \tag{5.21}$$

for all $\beta = (\beta_1, \ldots, \beta_{\ell'-1}) \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$. We claim that

the first summand on the right hand side of (5.21) is positive semidefinite and (5.22)

the second summand on the right hand side of (5.21) is positive definite. (5.23)

Clearly, if (5.22) and (5.23) hold then $(\partial^2 \mathbf{b})(\beta)$ is positive definite for all $\beta \in \times_{r=1}^{\ell'-1}(\beta_r^*, \infty)$.

Note that the first summand on the right hand side of (5.21) is the product of a scalar-valued function and a dyadic product function. Since the dyadic product is of the form $zz^\top$, it is positive semidefinite. Since $p_{\ell'}/(\partial p_{\ell'})^3 < 0$ (see (4.19)), statement (5.22) follows once we prove

$$(\partial p_{\ell'})^2 - p_{\ell'} \cdot \partial^2 p_{\ell'} \leq 0.$$

Note that the second summand on the right hand side of (5.21) is the product of a scalar-valued function and a diagonal matrix function. Since $p_{\ell'}/\partial p_{\ell'} < 0$ and $p_r^2 > 0$ for all $r \in \overline{1, \ell' - 1}$, statement (5.23) follows once we prove

$$(\partial p_r)^2 - p_r \cdot \partial^2 p_r < 0 \text{ for all } r \in \overline{1, \ell' - 1}.$$

Therefore, to prove (5.22) and (5.23), it suffices to prove that

$$(\partial p_r)^2 - p_r \cdot \partial^2 p_r < 0 \text{ for all } r \in \overline{1, \ell'}. \tag{5.24}$$

Fix $r \in \overline{1, \ell'}$. In order to ease the notation, we omit the index r in the rest of this proof. From (4.31), we have

$$\partial p = p \cdot H_1 \text{ and}$$
$$\partial^2 p = \partial p \cdot H_1 + p \cdot \partial H_1.$$

Hence,

$$(\partial p)^2 - p \cdot \partial^2 p = \partial p \cdot p \cdot H_1 - p \cdot \partial p \cdot H_1 - p^2 \cdot \partial H_1 = -p^2 \cdot \partial H_1 < 0,$$

where the last inequality follows from Proposition 4.18 (c). Hence, (5.24) indeed holds and this concludes the proof. □

5.5 Concluding remarks and directions of further research

We remark that the weak reversibility of the network became crucial in the proof of Theorem 5.2 only after Proposition 5.5. Indeed, since we did not restrict ourself in Section 4.2 to the weakly reversible case, Propositions 5.4 and 5.5 can be extended to the case $\ell = t$ (i.e., when all the linkage classes contain only one terminal strong linkage class) without any new idea. In case the network is of deficiency-one, but is *not* weakly reversible, a necessary condition to the non-emptiness of E_+ arises naturally (see Proposition 4.12). One might try to prove that this condition is also sufficient. The main difficulty in this case comes from the fact that if $(\mathcal{C}^r, \mathcal{R}^r)$ is not strongly connected for some $r \in \overline{1, \ell}$ then $\beta_r^* = 0$, see Section 4.2. Thus, the region D (see Figure 5.3), where we must search for the zeros of F is unbounded. Therefore, the Bolzano Theorem is not applicable directly. Also, one cannot expect in general that *each* positive stoichiometric class contains a positive steady state. A counterexample is the mass action system

$$X_1 \xrightarrow{\kappa_{12}} X_2 \tag{5.25}$$

$$2X_1 + X_2 \xrightarrow{\kappa_{34}} 3X_1,$$

which is taken from [27, (6.24)]. Denoting by E_0 the *set of boundary steady states*, i.e.,

$$E_0 = \{x \in \mathrm{bd}(\mathbb{R}^n_+) \mid B \cdot I_\kappa \cdot \Theta(x) = 0\},$$

a short calculation shows that

$$E_+ = \left\{ x = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \in \mathbb{R}^2_+ \;\middle|\; x_1 x_2 = \frac{\kappa_{12}}{\kappa_{34}} \right\} \text{ and}$$

$$E_0 = \left\{ x = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \in \mathrm{bd}(\mathbb{R}^2_+) \;\middle|\; x_1 = 0 \right\}.$$

We have depicted E_+ and E_0 in Figure 5.4. It is apparent that there exist positive stoichiometric classes, which do not contain any positive steady state. There is exactly one positive stoichiometric class with 1 positive steady state (which is unstable). Also, there exist positive stoichiometric classes, which contain 2 positive steady states (one of them is unstable, the other one is locally asymptotically stable relative to its positive stoichiometric class).

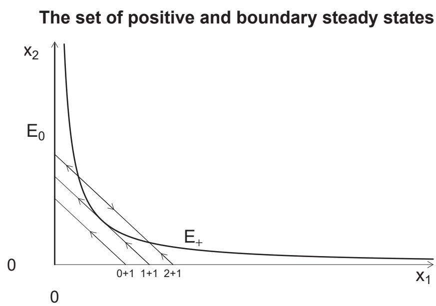


Figure 5.4: The set of positive and boundary steady states for the mass action system (5.25). The sums under the depicted positive stoichiometric classes indicate the number of positive steady states plus the number of boundary steady states in the respective positive stoichiometric class.

Results about non weakly reversible deficiency-one mass action systems would certainly be of interest, see e.g. the EnvZ-OmpR system in [52, Fig.2].

We remark that [48, Corollary 1 of Theorem 3] states that reversibility (which is a stronger condition than the weak reversibility) is sufficient for the existence of positive steady states in each positive stoichiometric class.

We have proven in this chapter that weakly reversible deficiency-one mass action systems possess the qualitative property that each positive stoichiometric class contains a positive steady state. We have also demonstrated at the beginning of this chapter by the analysis of Example (v) in Table 5.1 that uniqueness of the positive steady states does not hold generally. This raises the natural question of whether we can still prove the finiteness of positive steady states inside the positive stoichiometric classes. Actually, in [23] it is claimed that for weakly reversible mass action systems each positive stoichiometric class contains finitely many positive steady states. However, the concise explanation there relies on a property of analytic functions. Nevertheless, the zero set of a multivariate real analytic function can be much more intricate than the zero set of a univariate real analytic function. It suffices to mention the example

$$\mathbb{R}^2 \ni (x,y) \mapsto (x^2+y^2-1, x^2+y^2-1) \in \mathbb{R}^2.$$

Though the zero set of this non-identically zero real analytic function is compact in $\mathbb{R}^2$, it is not finite. We sketch in the next paragraph how one can prove the finiteness of the positive steady states for weakly reversible deficiency-one mass action systems with $\ell' \leq 2$ (recall the definition of ℓ' from Section 5.1). Since $1 \leq \ell' \leq \ell$, we can conclude that this finiteness property holds for networks with at most two linkage classes.

In case $\ell' = 1$, the finiteness property is a consequence of the Deficiency-One Theorem (even the uniqueness follows). Let the objects

$$D, F, \mathbf{0}, n, \mathbf{x}, q, S, \beta_1^*, \text{ and } \beta_1^{**}$$

be as in Sections 5.1, 5.2, and 5.3 and assume that $\ell' = 2$. It should be clear that the number of positive steady states in a positive stoichiometric class is at most the number of zeros of F in D (if $\beta \in D$ and $F(\beta) = \mathbf{0}$ then $\mathbf{x}(\beta) \in (q + \operatorname{ran} S) \cap \mathbb{R}^n_+$ is the positive steady state corresponding to β). However, in case $\ell' = 2$, the domain (and also the range) of F lies in a one-dimensional space. Clearly, F can be defined on the open interval (β_1^*, ∞) (and not only on $[0, \beta_1^{**}]$). The crucial observation is that F is then an analytic function. This follows if we apply an analytic version of the Implicit Function Theorem during the proof of Proposition 5.4. Since $F(\beta_1^{**}) < 0$, the function F is not identically zero. Therefore, F can have at most finitely many zeros in any compact interval. As a consequence, F has only finitely many zeros in $D = (0, \beta_1^{**}) \subseteq [0, \beta_1^{**}]$. Unfortunately, we cannot directly transfer the argument presented above for the case $\ell' \geq 3$, because, as we have already mentioned in the previous paragraph, the zero set of a multivariate real analytic function can be an infinite compact set. One possible way to overcome this issue might be to obtain some information about the (non)singularity of $(\partial F)(\beta)$ for $\beta \in D$.

Beside the finiteness of the positive steady states for weakly reversible deficiency-one mass action systems, several other questions may arise. A few of them are listed below. To formulate such questions, let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a weakly reversible deficiency-one reaction network. Also, for $\kappa : \mathcal{R} \to \mathbb{R}_+$ denote by E_+^κ the set of positive steady states of the mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$.

- Does there exist $\kappa : \mathcal{R} \to \mathbb{R}_+$ such that $|E_+^\kappa \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$? If so, is it possible to characterise these κ's?

- One might try to find an easily checkable equivalent condition to "for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $|E_+^\kappa \cap \mathcal{P}| = 1$ for each positive stoichiometric class $\mathcal{P}$".

- Investigation of the stability properties of the positive steady states is of interest.

5.6 The acyclic directed graph of the implications

We have depicted below the acyclic directed graph of the implications of this chapter. For the organising principle of this directed graph, see Section 2.8.

$$
\begin{tikzcd}
\text{T C.3} \arrow[r] & \text{T C.4} \arrow[r] & \text{T C.2} \arrow[d] & & \text{P 2.12} \arrow[ddll] \arrow[ddl] \\
 & & \text{T C.5} \arrow[d] & & \text{C 4.5} \arrow[dl] \\
\text{L 2.5} \arrow[r] & \text{L 5.3} \arrow[r] & \text{T 5.2} & \text{P 5.4} \arrow[l] & \text{P 2.7} \arrow[l] \\
\text{P 4.19} \arrow[dr] & & \begin{array}{c}\text{P 5.5}\\ \text{(a), (b), (c)}\end{array} \arrow[u] & & \text{D 2.9} \arrow[ul] \\
\text{P 4.18} \arrow[r] & \text{P 5.5 (d)} & & \text{C 4.10} \arrow[uul] \arrow[uu] \arrow[ul] & \text{T C.1} \arrow[uul]
\end{tikzcd}
$$

Chapter 6

The dependence of the existence of the positive steady states on the rate coefficients for deficiency-one mass action systems with single linkage class

Since in this chapter we are concerned with the dependence of the existence of the positive steady states on the rate coefficients (while the reaction network is fixed), we denote by E_+^κ the set of positive steady states of a mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$. Thus, we indicate κ in the notation. With this, for a mass action system $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ we have

$$E_+^\kappa = \{x \in \mathbb{R}_+^n \mid B \cdot I_\kappa \cdot \Theta(x) = 0\}.$$

We recall the *Deficiency-Zero Theorem* from Chapter 4 in the form most suitable for our purposes in this chapter (see Theorem 4.16 (a)).

Theorem 6.1 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a chemical reaction network with $\ell = t = 1$ and $\delta = 0$. Then the following statements hold.*

(a) If $(\mathcal{C}, \mathcal{R})$ is strongly connected then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$.

(b) If $(\mathcal{C}, \mathcal{R})$ is not *strongly connected then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa = \emptyset$.*

We also recall the Deficiency-One Theorem from Chapter 4. Before that, we repeat those notations, that were introduced in Subsection 4.3.2 especially for the purposes of the non weakly reversible case of the Deficiency-One Theorem. For a chemical reaction network with $\ell = t = 1$, denote by $\mathcal{C}'$ the set of those complexes, which are in the terminal strong linkage class of $(\mathcal{C}, \mathcal{R})$ and let $\mathcal{C}'' = \mathcal{C} \setminus \mathcal{C}'$. Let $c' = |\mathcal{C}'|$ and $c'' = |\mathcal{C}''|$ (thus, $c'' = c - c'$). With this, $I_\kappa \in \mathbb{R}^{c \times c}$, $\Theta : \mathbb{R}_{\geq 0}^n \to \mathbb{R}_{\geq 0}^c$, and any vector $v \in \mathbb{R}^c$ can be considered the block forms

$$I_\kappa = \begin{bmatrix} I'_\kappa & * \\ 0 & I''_\kappa \end{bmatrix} \in \mathbb{R}^{(c'+c'') \times (c'+c'')}, \quad \Theta = \begin{bmatrix} \Theta' \\ \Theta'' \end{bmatrix} : \mathbb{R}_{\geq 0}^n \to \mathbb{R}_{\geq 0}^{c'+c''}, \quad \text{and} \quad v = \begin{bmatrix} v' \\ v'' \end{bmatrix} \in \mathbb{R}^{c'+c''},$$

where $I'_\kappa \in \mathbb{R}^{c' \times c'}$, $\Theta' : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{c'}_{\geq 0}$, and $v' \in \mathbb{R}^{c'}$ correspond to the complexes in $\mathcal{C}'$, while $I''_\kappa \in \mathbb{R}^{c'' \times c''}$, $\Theta'' : \mathbb{R}^n_{\geq 0} \to \mathbb{R}^{c''}_{\geq 0}$, and $v'' \in \mathbb{R}^{c''}$ correspond to the complexes in $\mathcal{C}''$. There are several ways to prove that I''_κ is invertible (provided that $\mathcal{C}'' \neq \emptyset$), see Section 2.6.

Primarily, we are interested in this chapter in mass action systems for which $\ell = t = 1$ and $\delta = 1$ hold. For such systems, the linear subspace $\ker B \cap \operatorname{ran} I_\kappa$ is one-dimensional and does not depend on κ (recall from Section 2.7 that for systems with $\ell = t$ we have $\delta = \dim(\ker B \cap \operatorname{ran} I_\kappa)$). For systems that are moreover *not* weakly reversible, let us fix $h \in \mathbb{R}^c$ such that

$$0 \neq h \in \ker B \cap \operatorname{ran} I_\kappa \text{ and } h(\mathcal{C}'') \leq 0, \tag{6.1}$$

where the notation $h(\mathcal{C}'')$ is understood in accordance with (1.1), i.e., the sum of certain coordinates of h is non-positive, where the summation goes for those complexes that are out of the absorbing strong component of $(\mathcal{C}, \mathcal{R})$. It is important to note that h does not depend on κ.

With these notations in hand, we are ready to state the Deficiency-One Theorem in its augmented form (see Theorem 4.16, [11, Theorem III.7], and [12, Theorems 3.11 and 3.19]).

Theorem 6.2 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a chemical reaction network with $\ell = t = 1$ and $\delta = 1$. Then the following statements hold.*

(a) If $(\mathcal{C}, \mathcal{R})$ is strongly connected then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$.

(b) Assume that $(\mathcal{C}, \mathcal{R})$ is not *strongly connected. Let $h \in \mathbb{R}^c$ be as in (6.1) and fix $\kappa : \mathcal{R} \to \mathbb{R}_+$. Then*

$E_+^\kappa \neq \emptyset$ if and only if all the coordinates of $(I''_\kappa)^{-1} h''$ are positive.

As it was discussed in Subsection 4.3.2, the choice of h in (6.1) does not affect the condition $(I''_\kappa)^{-1} h'' \in \mathbb{R}^{c''}_+$.

As a side remark, we also mention that both in Theorems 6.1 and 6.2, once $E_+^\kappa \neq \emptyset$ holds, there is exactly one positive steady state in each positive stoichiometric class (see Theorem 4.16).

Thus, if the reaction network satisfies $\ell = t = 1$ and $\delta = 0$ then the non-emptiness of E_+^κ does not depend on κ. Also, if the reaction network satisfies $\ell = t = 1$ and $\delta = 1$, and moreover $(\mathcal{C}, \mathcal{R})$ is strongly connected then, again, the non-emptiness of E_+^κ does not depend on κ. However, by Theorem 6.2 (b), we have a different situation for mass action systems for which the underlying reaction network satisfies $\ell = t = 1$ and $\delta = 1$, but $(\mathcal{C}, \mathcal{R})$ is *not* strongly connected. For these mass action systems, the non-emptiness of E_+^κ *may* depend on κ. We used the word "may", because three different kind of phenomena can occur when rate coefficients are assigned to a single linkage class deficiency-one reaction network that is not weakly reversible:

- $E_+^\kappa \neq \emptyset$ for all κ (i.e., for all κ all the coordinates of $(I''_\kappa)^{-1} h''$ are positive),
- $E_+^\kappa = \emptyset$ for all κ (i.e., for all κ there exists a non-positive coordinate of $(I''_\kappa)^{-1} h''$), and
- the non-emptiness of E_+^κ depends on κ (i.e., there exists a κ such that all the coordinates of $(I''_\kappa)^{-1} h''$ are positive and there also exists a κ such that there exists a non-positive coordinate of $(I''_\kappa)^{-1} h''$).

It was demonstrated in Chapter 4 that all of these three phenomena can indeed occur (see (4.2), (4.3), and (4.4) and their analysis in Subsection 4.3.2). The aim of this chapter is to provide characterisations of the above cases. Namely, we will formulate equivalent conditions to the statements

$$\text{“there exists a } \kappa : \mathcal{R} \to \mathbb{R}_+ \text{ such that } E_+^\kappa \neq \emptyset\text{” and} \tag{6.2}$$

$$\text{“for all } \kappa : \mathcal{R} \to \mathbb{R}_+ \text{ we have } E_+^\kappa \neq \emptyset\text{”.} \tag{6.3}$$

In Section 6.1, we examine the above questions under some extra assumptions on $(\mathcal{C}, \mathcal{R})$. In Subsection 6.1.1, we will assume that $(\mathcal{C}, \mathcal{R})$ is a “chain”. As a generalisation of the results of Subsection 6.1.1, we will assume in Subsection 6.1.2 that $(\mathcal{C}, \mathcal{R})$ is “tree-like”. As a matter of fact, we will obtain a recursive formula for the coordinates of $(I''_\kappa)^{-1}h''$ (the matrix I''_κ has some special properties in these cases, which makes it possible to handle the computation of its inverse). Based on the obtained recursive formula, we will deduce equivalent conditions both for (6.2) and (6.3). In Sections 6.2 and 6.3, we will assume only that $(\mathcal{C}, \mathcal{R})$ satisfies $\ell = t = 1$, but is *not* strongly connected. Under this assumption, we provide equivalent conditions to (6.2) and (6.3) for these general cases in Sections 6.2 and 6.3, respectively.

In this chapter, we need more involved graph theoretical arguments. Therefore, we have collected the required graph theoretical notions in Appendix A.

6.1 Special cases

We always assume in the rest of this chapter that the reaction network under consideration satisfies $\ell = t = 1$ and $\delta = 1$, but is *not* strongly connected. Thus, $\mathcal{C}'' \neq \emptyset$. Since we will apply Theorem 6.2 (b), we fix $h \in \mathbb{R}^c$ as in (6.1) (recall that $\ell = t$ implies that $\operatorname{ran} I_\kappa$ does not depend on κ, and hence, h is not influenced by κ). Also, let $\vartheta \in \mathbb{R}^c$ be such that

$$I_\kappa \vartheta = h. \tag{6.4}$$

Thus, ϑ depends on κ. Since I_κ is block upper triangular, we obtain that $I''_\kappa \vartheta'' = h''$. Thus, $\vartheta'' = (I''_\kappa)^{-1}h''$. By Theorem 6.2 ($b$), we have

$$E_+^\kappa \neq \emptyset \text{ if and only if } \vartheta'' \in \mathbb{R}_+^{c''}. \tag{6.5}$$

Thus, our aim in this section is to obtain a formula for the coordinates of ϑ''.

Let us recall (the purely graph theoretical) Proposition 2.3. It will be useful in Subsections 6.1.1 and 6.1.2.

Lemma 6.3 *Let (V, A) be a directed graph and let $\vartheta : V \to \mathbb{R}$ be any function. Let $\kappa : V \times V \to \mathbb{R}_{\geq 0}$ be a function for which $\kappa_{ij} > 0$ if and only if $(i, j) \in A$. Define $z : A \to \mathbb{R}$ by $z_{ij} = \kappa_{ij}\vartheta_i$ $((i, j) \in A)$, let I_κ be as in (2.8), and let $h = I_\kappa \vartheta$. Then*

$$\operatorname{excess}_z(U) = \sum_{j \in U} h_j \text{ for all } U \subseteq V.$$

6.1.1 The case $(\mathcal{C},\mathcal{R})$ is a "chain"

Assume for this subsection that the graph of complexes (i.e., $(\mathcal{C},\mathcal{R})$) takes the special form

$$C_c \underset{\kappa_{c-1,c}}{\overset{\kappa_{c,c-1}}{\rightleftarrows}} C_{c-1} \underset{\kappa_{c-2,c-1}}{\overset{\kappa_{c-1,c-2}}{\rightleftarrows}} \cdots \underset{\kappa_{34}}{\overset{\kappa_{43}}{\rightleftarrows}} C_3 \underset{\kappa_{23}}{\overset{\kappa_{32}}{\rightleftarrows}} C_2 \xrightarrow{\kappa_{21}} C_1, \qquad (6.6)$$

where we also indicated the rate coefficients. Note that in this case $\mathcal{C}' = \{C_1\}$ and $\mathcal{C}'' = \{C_2,\ldots,C_c\}$, while the matrix I''_κ is tridiagonal and moreover

$$\text{the column sums of } I''_\kappa \text{ are zero except the one corresponding to } C_2. \qquad (6.7)$$

Clearly, (6.7) is a consequence of the fact that leaving the set $\mathcal{C}''$ is only possible through C_2 (i.e., using the notations introduced in Appendix A, $\emptyset \neq \varrho^{\text{out}}(\mathcal{C}'') \subseteq \varrho^{\text{out}}(C_2)$). Proposition 6.4 below provides a recursive formula for the coordinates of ϑ''.

Proposition 6.4 *Let $(\mathcal{X},\mathcal{C},\mathcal{R},\kappa)$ be a deficiency-one mass action system for which $(\mathcal{C},\mathcal{R})$ takes the form* (6.6)*. Let h and ϑ be as in* (6.1) *and* (6.4)*, respectively. Then*

$$\vartheta_2 = -\frac{1}{\kappa_{21}}\sum_{i=2}^{c} h_i \text{ and} \qquad (6.8)$$

$$\vartheta_j = \frac{\kappa_{j-1,j}}{\kappa_{j,j-1}}\vartheta_{j-1} - \frac{1}{\kappa_{j,j-1}}\sum_{i=j}^{c} h_i \quad (j=3,\ldots,c). \qquad (6.9)$$

Proof Application of Lemma 6.3 with $U=\mathcal{C}''$ yields $-\kappa_{21}\vartheta_2 = \sum_{i=2}^{c} h_i$. This proves (6.8).

Fix $j\in\{3,\ldots,c\}$. Application of Lemma 6.3 with $U=\{C_j,\ldots,C_c\}$ yields

$$\kappa_{j-1,j}\vartheta_{j-1} - \kappa_{j,j-1}\vartheta_j = \sum_{i=j}^{c} h_i.$$

This proves (6.9). □

As a corollary of Proposition 6.4, we directly obtain a characterisation of those deficiency-one reaction networks with graph of complexes (6.6) for which there exist rate coefficients such that the resulting mass action system has a positive steady state. Similarly, a characterisation is given for those networks for which the resulting mass action system has a positive steady state regardless of the values of the rate coefficients.

Corollary 6.5 *Let $(\mathcal{X},\mathcal{C},\mathcal{R})$ be a deficiency-one reaction network for which $(\mathcal{C},\mathcal{R})$ takes the form* (6.6)*. Let $h\in\mathbb{R}^c$ be as in* (6.1)*. Then there exists a $\kappa:\mathcal{R}\to\mathbb{R}_+$ such that $E_+^\kappa\neq\emptyset$ if and only if*

$$\sum_{i=2}^{c} h_i < 0.$$

Proof The statement directly follows from (6.5) and Proposition 6.4. □

Corollary 6.6 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a deficiency-one reaction network for which $(\mathcal{C}, \mathcal{R})$ takes the form* (6.6)*. Let $h \in \mathbb{R}^c$ be as in* (6.1)*. Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$ if and only if*

$$\sum_{i=2}^{c} h_i < 0 \text{ and}$$

$$\sum_{i=j}^{c} h_i \leq 0 \text{ for all } j \in \{3, \ldots, c\}.$$

Proof The statement directly follows from (6.5) and Proposition 6.4. □

6.1.2 The case $(\mathcal{C}, \mathcal{R})$ is "tree-like"

In this subsection, we generalise the results obtained in Subsection 6.1.1. We will not pose in this subsection the condition that the graph of complexes $(\mathcal{C}, \mathcal{R})$ takes the form (6.6), rather we assume that $(\mathcal{C}, \mathcal{R})$ satisfies

$$\ell = t = 1 \text{ and } (\mathcal{C}, \mathcal{R}) \text{ is not strongly connected,} \tag{6.10}$$

$$\text{there exists a unique } l \in \mathcal{C}'' \text{ such that } \varrho^{\text{out}}(l) \cap \varrho^{\text{out}}(\mathcal{C}'') \neq \emptyset, \text{ and} \tag{6.11}$$

$$\text{for all } i \in \mathcal{C}'' \text{ there exists a unique directed path from } i \text{ to } l. \tag{6.12}$$

Thus, by (6.11), we have $\emptyset \neq \varrho^{\text{out}}(\mathcal{C}'') \subseteq \varrho^{\text{out}}(l)$. Consider that the graph of complexes $(\mathcal{C}, \mathcal{R})$ takes the form

$$\begin{tikzcd}
C_{17} \arrow[r, shift left] \arrow[r, leftarrow, shift right] & C_{16} \arrow[dr, shift left] \arrow[dr, leftarrow, shift right] & C_{10} \arrow[r] & C_9 \arrow[r, shift left] \arrow[r, leftarrow, shift right] & C_8 \arrow[dr] & & C_1 \arrow[d] & C_6 \arrow[l] \\
C_{18} \arrow[ur] & C_{21} \arrow[dr] & C_{15} \arrow[dr] & C_{11} \arrow[ur] & C_{12} \arrow[r] & C_7 \arrow[ur] \arrow[r] \arrow[dr] & C_2 \arrow[d] & C_5 \arrow[u] \\
C_{19} \arrow[uur] & C_{22} \arrow[r, shift left] \arrow[r, leftarrow, shift right] & C_{20} \arrow[r] & C_{14} \arrow[r] & C_{13} \arrow[ur, shift left] \arrow[ur, leftarrow, shift right] & & C_3 \arrow[r] & C_4 \arrow[u] .
\end{tikzcd} \tag{6.13}$$

Note that $\mathcal{C}' = \{C_1, \ldots, C_6\}$ and $\mathcal{C}'' = \{C_7, \ldots, C_{22}\}$ for (6.13). Also, (6.13) satisfies (6.10), (6.11), and (6.12) with $l = C_7$.

Clearly, the graph in (6.6) satisfies (6.10), (6.11), and (6.12) with $l = C_2$. Thus, the results of this subsection are indeed generalisations of the results of Subsection 6.1.1.

For $j \in \mathcal{C}''$ denote by P_j the unique directed path from j to l and for $i \in \mathcal{C}''$ define $U(i) \subseteq \mathcal{C}''$, called the *set of descendants* of i, by

$$U(i) = \{j \in \mathcal{C}'' \mid i \in V[P_j]\},$$

i.e., we collect those vertices for which the unique directed path to l traverses i. Also, for $j \in \mathcal{C}'' \backslash \{l\}$ define $p(j) \in V[P_j]$, called the *parent* of j, by the implicit definition

$$\text{len}(P_{p(j)}) = \text{len}(P_j) - 1,$$

i.e., the parent of j is the second vertex on the unique directed path from j to l. For example, for (6.13) we have $p(C_{20}) = C_{14}$ and $U(C_{20}) = \{C_{20}, C_{21}, C_{22}\}$.

We are now ready to state and prove the generalisation of Proposition 6.4.

Proposition 6.7 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R}, \kappa)$ be a deficiency-one mass action system for which $(\mathcal{C}, \mathcal{R})$ satisfies* (6.10), (6.11), *and* (6.12). *Let h and ϑ be as in* (6.1) *and* (6.4), *respectively. Then*

$$\vartheta_l = -\frac{1}{\sum_{l' \in \mathcal{C}'} \kappa_{l,l'}} \sum_{i \in \mathcal{C}''} h_i, \tag{6.14}$$

$$\vartheta_j = \frac{\kappa_{p(j),j}}{\kappa_{j,p(j)}} \vartheta_{p(j)} - \frac{1}{\kappa_{j,p(j)}} \sum_{i \in U(j)} h_i \quad (j \in \mathcal{C}'' \backslash \{l\}). \tag{6.15}$$

Proof Application of Lemma 6.3 with $U = \mathcal{C}''$ yields $-\sum_{l' \in \mathcal{C}'} \kappa_{l,l'} \vartheta_l = \sum_{i \in \mathcal{C}''} h_i$. This proves (6.14).

Fix $j \in \mathcal{C}'' \backslash \{l\}$. Application of Lemma 6.3 with $U = U(j)$ yields

$$\kappa_{p(j),j} \vartheta_{p(j)} - \kappa_{j,p(j)} \vartheta_j = \sum_{i \in U(j)} h_i.$$

This proves (6.15). □

As consequences of Proposition 6.7, we directly obtain the generalisations of Corollaries 6.5 and 6.6.

Corollary 6.8 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a deficiency-one reaction network for which $(\mathcal{C}, \mathcal{R})$ satisfies* (6.10), (6.11), *and* (6.12). *Let $h \in \mathbb{R}^c$ be as in* (6.1). *Then there exists a $\kappa : \mathcal{R} \to \mathbb{R}_+$ such that $E_+^\kappa \neq \emptyset$ if and only if*

$$\sum_{i \in \mathcal{C}''} h_i < 0 \text{ and}$$
$$\sum_{i \in U(j)} h_i < 0 \text{ for all } j \in \mathcal{C}'' \backslash \{l\} \text{ that satisfies } \kappa_{p(j),j} = 0.$$

Proof The statement directly follows from (6.5) and Proposition 6.7. □

Corollary 6.9 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a deficiency-one reaction network for which $(\mathcal{C}, \mathcal{R})$ satisfies* (6.10), (6.11), *and* (6.12). *Let $h \in \mathbb{R}^c$ be as in* (6.1). *Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$ if and only if*

$$\sum_{i \in \mathcal{C}''} h_i < 0,$$
$$\sum_{i \in U(j)} h_i < 0 \text{ for all } j \in \mathcal{C}'' \backslash \{l\} \text{ that satisfies } \kappa_{p(j),j} = 0, \text{ and}$$
$$\sum_{i \in U(j)} h_i \leq 0 \text{ for all } j \in \mathcal{C}'' \backslash \{l\} \text{ that satisfies } \kappa_{p(j),j} > 0.$$

Proof The statement directly follows from (6.5) and Proposition 6.7. □

Note that for (6.13) we have

$$\kappa_{p(j),j} = 0 \text{ for } j \in \{C_8, C_{10}, C_{11}, C_{12}, C_{14}, C_{15}, C_{18}, C_{19}, C_{20}, C_{21}\} \text{ and}$$
$$\kappa_{p(j),j} > 0 \text{ for } j \in \{C_9, C_{13}, C_{16}, C_{17}, C_{22}\}.$$

Thus, application of Corollary 6.8 yields for (6.13) that there exists a $\kappa : \mathcal{R} \to \mathbb{R}_+$ such that $E_+^\kappa \neq \emptyset$ if and only if

$$\begin{aligned}&h_7 + \cdots + h_{22} < 0, h_8 + \cdots + h_{11} < 0, h_{10} < 0, h_{11} < 0, h_{12} < 0, h_{14} + \cdots + h_{22} < 0,\\ &h_{15} + \cdots + h_{19} < 0, h_{18} < 0, h_{19} < 0, h_{20} + h_{21} + h_{22} < 0, \text{ and } h_{21} < 0.\end{aligned} \tag{6.16}$$

Similarly, application of Corollary 6.9 yields for (6.13) that for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$ if and only if

$$\begin{aligned}&\text{(6.16) holds and moreover}\\ &h_9 + h_{10} \leq 0, h_{13} + \cdots + h_{22} \leq 0, h_{16} + \cdots + h_{19} \leq 0, h_{17} \leq 0, h_{22} \leq 0.\end{aligned}$$

6.2 The existence of rate coefficients such that the set of positive steady states is nonempty

In this section we generalise Corollary 6.8. We will assume only that the reaction network under consideration is of deficiency-one and satisfies (6.10). The main tool we use is the following purely graph theoretical theorem. We also provide its proof below after some preparations. The graph theoretical notions and notations appearing in the sequel are summarised in Appendix A.

Theorem 6.10 *Let (V, A) be a weakly connected directed graph and let $h : V \to \mathbb{R}$ be a function with $h(V) = 0$. Then there exists an h-transshipment $z : A \to \mathbb{R}_+$ if and only if*

$$h(U) < 0 \textit{ for all } \emptyset \neq U \subsetneq V \textit{ with } \varrho^{\text{in}}(U) = \emptyset. \tag{6.17}$$

The main tool we will use to prove Theorem 6.10 is the following theorem (see [51, Corollary 11.2f]), which is a well-known consequence of the Hoffman's Theorem (see [51, Theorem 11.2]).

Theorem 6.11 *Let (V, A) be a directed graph, let $d, c : A \to \mathbb{R}$ with $d \leq c$ and let $h : V \to \mathbb{R}$ with $h(V) = 0$. Then there exists an h-transshipment z with $d \leq z \leq c$ if and only if*

$$c(\varrho^{\text{in}}(U)) - d(\varrho^{\text{out}}(U)) \geq h(U) \textit{ for all } U \subseteq V.$$

Note that Theorem 6.10 characterises the existence of a *positive* h-transshipment for a function $h : V \to \mathbb{R}$ with $h(V) = 0$. Compare this to the characterisation of the existence of a *nonnegative* h-transshipment (see [51, Corollary 11.2h]).

Proof of Theorem 6.10 To show that (6.17) is necessary, let $z : A \to \mathbb{R}_+$ be an h-transshipment and $\emptyset \neq U \subsetneq V$ with $\varrho^{\text{in}}(U) = \emptyset$. Then

$$h(U) = \text{excess}_z(U) = z(\varrho^{\text{in}}(U)) - z(\varrho^{\text{out}}(U)) = -z(\varrho^{\text{out}}(U)) < 0,$$

where the inequality holds, because $\varrho^{\text{out}}(U)$ and $\varrho^{\text{in}}(U)$ cannot be empty at the same time ((V, A) is assumed to be weakly connected and $\emptyset \neq U \subsetneq V$) and the values of z are positive.

To show the sufficiency of (6.17), assume for the rest of this proof that (6.17) holds. Clearly, the existence of a positive h-transshipment is equivalent to the existence of $0 < \varepsilon \leq K$ such that there exists an h-transshipment z with $\varepsilon \leq z \leq K$. By Theorem 6.11, the latter is equivalent to the existence of $0 < \varepsilon \leq K$ such that

$$K|\varrho^{\text{in}}(U)| - \varepsilon|\varrho^{\text{out}}(U)| \geq h(U) \text{ for all } U \subseteq V. \tag{6.18}$$

Let

$$\varepsilon = \min\left(\left\{-\frac{h(U)}{|\varrho^{\text{out}}(U)|} \;\middle|\; \emptyset \neq U \subsetneq V \text{ and } \varrho^{\text{in}}(U) = \emptyset\right\} \bigcup \{1\}\right) \text{ and} \tag{6.19}$$

$$K = \max\left(\left\{\frac{h(U) + \varepsilon|\varrho^{\text{out}}(U)|}{|\varrho^{\text{in}}(U)|} \;\middle|\; \emptyset \neq U \subsetneq V \text{ and } \varrho^{\text{in}}(U) \neq \emptyset\right\} \bigcup \{\varepsilon\}\right). \tag{6.20}$$

Note that $\varepsilon > 0$ is guaranteed by (6.17). Also, we have $\varepsilon \leq K$. We show that (6.18) holds with these specific choices of ε and K.

Both for $U = \emptyset$ and $U = V$ we have $\varrho^{\text{in}}(U) = \varrho^{\text{out}}(U) = \emptyset$ and $h(U) = 0$, hence (6.18) holds in both cases.

Fix for the rest of this proof $\emptyset \neq U \subsetneq V$. In case $\varrho^{\text{in}}(U) = \emptyset$, (6.18) is a consequence of (6.19), while in case $\varrho^{\text{in}}(U) \neq \emptyset$, (6.18) follows from (6.20). □

As a corollary of Theorem 6.10, we obtain the generalisation of Corollary 6.8.

Corollary 6.12 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network for which $\ell = t = 1$ and $\delta = 1$. Assume that $(\mathcal{C}, \mathcal{R})$ is not strongly connected and let $h \in \mathbb{R}^c$ be as in (6.1). Then there exists a $\kappa : \mathcal{R} \to \mathbb{R}_+$ such that $E_+^\kappa \neq \emptyset$ if and only if*

$$h(\widetilde{\mathcal{C}}) < 0 \textit{ for all } \emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C} \textit{ with } \varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset. \tag{6.21}$$

Proof To prove that (6.21) is necessary, let $\kappa : \mathcal{R} \to \mathbb{R}_+$ be such that $E_+^\kappa \neq \emptyset$. Then, by Theorem 6.2 (*b*), we have $(I_\kappa'')^{-1}h'' \in \mathbb{R}_+^{c''}$. Let $\vartheta \in \mathbb{R}^c$ be such that $I_\kappa \vartheta = h$ and define $z : \mathcal{R} \to \mathbb{R}$ by $z_{ij} = \kappa_{ij}\vartheta_i$. Since $\vartheta'' = (I_\kappa'')^{-1}h''$, we have $\vartheta_i'' > 0$ for all $i \in \mathcal{C}''$. Also, let $\emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C}$ be such that $\varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset$. Then clearly $\widetilde{\mathcal{C}} \subseteq \mathcal{C}''$ and $\varrho^{\text{out}}(\widetilde{\mathcal{C}}) \neq \emptyset$. Thus, by Lemma 6.3, we have

$$h(\widetilde{\mathcal{C}}) = \text{excess}_z(\widetilde{\mathcal{C}}) = -z(\varrho^{\text{out}}(\widetilde{\mathcal{C}})) = -\sum_{(i,j) \in \varrho^{\text{out}}(\widetilde{\mathcal{C}})} \kappa_{ij}\vartheta_i < 0.$$

To prove the sufficiency of (6.21), let $\kappa : \mathcal{R} \to \mathbb{R}_+$ be such that $\text{excess}_\kappa = h$ (see Theorem 6.10). Also, define $\vartheta \in \mathbb{R}^c$ by $\vartheta_i = 1$ ($i \in \mathcal{C}$). Then clearly $I_\kappa \vartheta = h$ (recall (2.8)). Thus, $(I_\kappa'')^{-1}h'' = \vartheta'' \in \mathbb{R}_+^{c''}$ and therefore Theorem 6.2 (*b*) concludes the proof. □

Consider that the graph of complexes takes the form

$$\begin{tikzcd} & C_6 \arrow[r, shift left] & C_5 \arrow[l, shift left] \arrow[r] & C_1 \arrow[r] & C_4 \arrow[d] \\ C_7 \arrow[ur] \arrow[r] & C_8 \arrow[r] & C_9 \arrow[ur] & C_2 \arrow[u] & C_3. \arrow[l] \end{tikzcd} \tag{6.22}$$

Application of Corollary 6.12 to a reaction network for which the graph of complexes is (6.22) yields that there exists a $\kappa : \mathcal{R} \to \mathbb{R}_+$ such that $E_+^\kappa \neq \emptyset$ if and only if

$$h_5 + h_6 + h_7 < 0, h_7 < 0, h_7 + h_8 < 0, h_7 + h_8 + h_9 < 0,$$
$$h_5 + h_6 + h_7 + h_8 < 0, \text{ and } h_5 + h_6 + h_7 + h_8 + h_9 < 0.$$

By Corollary 6.12, the sets of interest are $\emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C}$ for which $\varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset$. Therefore, we conclude this section by some comments about these sets (see Proposition 6.13 and Corollary 6.14 below). To this end, let us define for $i \in \mathcal{C}''$ the set $R(i) \subseteq \mathcal{C}''$ by

$$R(i) = \{j \in \mathcal{C}'' \mid \text{there exists a directed path from } j \text{ to } i \text{ in } (\mathcal{C}, \mathcal{R})\}. \tag{6.23}$$

Recall from Section 2.5 that the strong components of the directed graph $(\mathcal{C}, \mathcal{R})$ are called the strong linkage classes in CRNT.

Proposition 6.13 *Assume that $(\mathcal{C}, \mathcal{R})$ satisfies (6.10) and for $i \in \mathcal{C}''$ let $R(i)$ be as in (6.23). Then*

(a) for all $i \in \mathcal{C}''$ we have $i \in R(i)$,

(b) for all $i \in \mathcal{C}''$ the set $R(i)$ is the disjoint union of some strong linkage classes,

(c) if $i_1 \in \mathcal{C}''$ and $i_2 \in \mathcal{C}''$ are in the same strong linkage class then $R(i_1) = R(i_2)$,

(d) for all $i \in \mathcal{C}''$ we have $\emptyset \neq R(i) \subsetneq \mathcal{C}$ and $\varrho^{\text{in}}(R(i)) = \emptyset$,

(e) if $\emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C}$ is such that $\varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset$ and $i \in \widetilde{\mathcal{C}}$ then $R(i) \subseteq \widetilde{\mathcal{C}}$, and

(f) for all $i_1, i_2 \in \mathcal{C}''$ we have $\emptyset \neq R(i_1) \cup R(i_2) \subsetneq \mathcal{C}$ and $\varrho^{\text{in}}(R(i_1) \cup R(i_2)) = \emptyset$.

Proof All the statements are trivial. □

Corollary 6.14 *Assume that $(\mathcal{C}, \mathcal{R})$ satisfies (6.10) and for $i \in \mathcal{C}''$ let $R(i)$ be as in (6.23). Let $\emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C}$ be such that $\varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset$. Then there exists a $J \subseteq \mathcal{C}''$ such that $\widetilde{\mathcal{C}} = \cup_{i \in J} R(i)$.*

Proof The statement directly follows from Proposition 6.13 (a) and (e). □

For (6.22) we have

$$R(5) = R(6) = \{5, 6, 7\}, R(7) = \{7\}, R(8) = \{7, 8\}, \text{ and } R(9) = \{7, 8, 9\}.$$

It can be seen that the sets $\emptyset \neq \widetilde{\mathcal{C}} \subsetneq \mathcal{C}$ for which $\varrho^{\text{in}}(\widetilde{\mathcal{C}}) = \emptyset$ holds for (6.22) are exactly the sets

$$R(5), R(7), R(8), R(9), R(5) \cup R(8), \text{ and } R(5) \cup R(9).$$

6.3 The non-emptiness of the set of positive steady states regardless of the values of the rate coefficients

We generalised Corollary 6.8 in Section 6.2. Our aim in the present section is to generalise Corollary 6.9. Namely, to provide an equivalent condition to the statement "for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$" for deficiency-one reaction networks for which the graph of complexes satisfies (6.10). By Theorem 6.2 (*b*), the important object is $(I''_\kappa)^{-1}h''$, thus it does not restrict the generality if we contract the absorbing strong component of $(\mathcal{C}, \mathcal{R})$ into one vertex. So assume throughout this section that

$$\mathcal{C}' \text{ is a singleton.}$$

Also, in order to ease the notation, we identify the set $\mathcal{C}'$ with the sole element in that set. (Though it is straightforward to extend all the definitions, proofs, and results of this section to the case $|\mathcal{C}'| \geq 2$, we still suppose $|\mathcal{C}'| = 1$ in order to avoid unnecessary technical complications.)

The rest of this section is organised as follows. After providing a formula for the entries of $(I''_\kappa)^{-1}$ (see Theorem 6.15), we prove the generalisation of Corollary 6.9 (see Corollary 6.16). As it will be demonstrated on the example (6.31), the obtained result contains certain redundancies. We will get rid of these redundancies in three steps (see Corollaries 6.20, 6.25, 6.26). After some further manipulations, we arrive to Theorem 6.28, which is the main result of this chapter. Finally, we provide some additional results related to the condition that appears in Theorem 6.28 (see Propositions 6.29 and 6.30).

We first provide a formula for the entries of the inverse of I''_κ via the Matrix-Tree Theorem. This formula in some other context and with slightly different notations also appears in [47, Appendix]. Please refer to Appendix D for more on the Matrix-Tree Theorem.

Theorem 6.15 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10). *Fix* $i, j \in \mathcal{C}''$. *Then*

$$((I''_\kappa)^{-1})_{ji} = -\frac{\sum_{\widetilde{\mathcal{R}} \in \mathcal{T}^{ij}_{\mathcal{D}}(\mathcal{C}' \cup \{j\})} \kappa_{\widetilde{\mathcal{R}}}}{\sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}')} \kappa_{\widetilde{\mathcal{R}}}}, \tag{6.24}$$

where the summation in the enumerator goes for those $(\mathcal{C}' \cup \{j\})$*-branchings* $\widetilde{\mathcal{R}}$ *in* $\mathcal{D} = (\mathcal{C}, \mathcal{R})$ *for which there exists a directed path from* i *to* j *in* $(\mathcal{C}, \widetilde{\mathcal{R}})$*, while the summation in the denominator goes for the* $\mathcal{C}'$*-branchings* $\widetilde{\mathcal{R}}$ *in* $\mathcal{D} = (\mathcal{C}, \mathcal{R})$ *(see Appendix A for the definitions of these standard graph theoretical terms). The symbol* $\kappa_{\widetilde{\mathcal{R}}}$ *is a shorthand notation for the product* $\prod_{a \in \widetilde{\mathcal{R}}} \kappa_a$.

Proof Application of Theorem D.3 to the transpose of I_κ twice yield

$$((I''_\kappa)^{-1})_{ji} = ((I''^{\top}_\kappa)^{-1})_{ij} = \frac{(-1)^{i+j} d_{ji}(I''^{\top}_\kappa)}{\det I''^{\top}_\kappa} = \frac{(-1)^{i+j} d_{\mathcal{C}' \cup \{j\}, \mathcal{C}' \cup \{i\}}(I^\top_\kappa)}{d_{\mathcal{C}', \mathcal{C}'}(I^\top_\kappa)} =$$
$$= \frac{(-1)^{c-|\mathcal{C}'|-1} \sum_{\widetilde{\mathcal{R}} \in \mathcal{T}^{ij}_{\mathcal{D}}(\mathcal{C}' \cup \{j\})} \kappa_{\widetilde{\mathcal{R}}}}{(-1)^{c-|\mathcal{C}'|} \sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}')} \kappa_{\widetilde{\mathcal{R}}}},$$

where $d_{Q_1,Q_2}(Z)$ denotes the determinant of that matrix, which is obtained from Z by deleting the rows with index in Q_1 and the columns with index in Q_2. $\square$

See Figure 6.1 for an illustration of the notions appearing in Theorem 6.15.

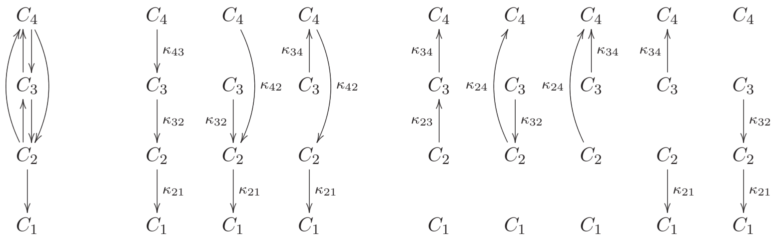


Figure 6.1: An example of a graph of complexes $\mathcal{D} = (\mathcal{C}, \mathcal{R})$ with $\mathcal{C} = \{C_1, C_2, C_3, C_4\}$ and $\mathcal{C}' = \{C_1\}$ (on the left), the three 1-branchings in $\mathcal{D}$ (in the middle), and the five $\{1,4\}$-branchings in $\mathcal{D}$ (on the right). Note that $|\mathcal{T}_{\mathcal{D}}^{24}(\{1,4\})| = 3$, $|\mathcal{T}_{\mathcal{D}}^{34}(\{1,4\})| = 4$, and $|\mathcal{T}_{\mathcal{D}}^{44}(\{1,4\})| = 5$. Thus, e.g. for $i = 2$ and $j = 4$ the enumerator in (6.24) is the sum of 3 products and each of these products has 2 factors, namely, $\kappa_{23}\kappa_{34} + \kappa_{24}\kappa_{32} + \kappa_{24}\kappa_{34}$.

Let us introduce the notation $L_{\mathcal{D}}(\kappa) = \sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}')} \kappa_{\widetilde{\mathcal{R}}}$. Thus, e.g. for the example in Figure 6.1 we have

$$L_{\mathcal{D}}(\kappa) = \kappa_{21}\kappa_{32}\kappa_{43} + \kappa_{21}\kappa_{32}\kappa_{42} + \kappa_{21}\kappa_{34}\kappa_{42}.$$

From this point on, let h and ϑ be as in (6.1) and (6.4), respectively. As a consequence of Theorem 6.15, for $j \in \mathcal{C}''$ we have

$$\begin{aligned}\vartheta_j = \left[(I''_\kappa)^{-1}h''\right]_j &= -\frac{1}{L_{\mathcal{D}}(\kappa)} \sum_{i \in \mathcal{C}''} h_i \left(\sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}^{ij}(\mathcal{C}' \cup \{j\})} \kappa_{\widetilde{\mathcal{R}}} \right) = \\ &= -\frac{1}{L_{\mathcal{D}}(\kappa)} \sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}' \cup \{j\})} \left(\kappa_{\widetilde{\mathcal{R}}} \cdot h(V[\widetilde{\mathcal{R}}, j]) \right),\end{aligned}$$

where $V[\widetilde{\mathcal{R}}, j]$ denotes the vertex set of the j-arborescence of the $(\mathcal{C}' \cup \{j\})$-branching $\widetilde{\mathcal{R}}$ (see Appendix A). As an illustration of the equality

$$\sum_{i \in \mathcal{C}''} h_i \left(\sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}^{ij}(\mathcal{C}' \cup \{j\})} \kappa_{\widetilde{\mathcal{R}}} \right) = \sum_{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}' \cup \{j\})} \left(\kappa_{\widetilde{\mathcal{R}}} \cdot h(V[\widetilde{\mathcal{R}}, j]) \right)$$

for $j = 4$ for the example in Figure 6.1, we have

$$\begin{aligned}&h_2(\kappa_{23}\kappa_{34} + \kappa_{24}\kappa_{32} + \kappa_{24}\kappa_{34}) + \\ &+ h_3(\kappa_{23}\kappa_{34} + \kappa_{24}\kappa_{32} + \kappa_{24}\kappa_{34} + \kappa_{21}\kappa_{34}) + \\ &+ h_4(\kappa_{23}\kappa_{34} + \kappa_{24}\kappa_{32} + \kappa_{24}\kappa_{34} + \kappa_{21}\kappa_{34} + \kappa_{21}\kappa_{32})\end{aligned}$$

on the left hand side and

$$\begin{aligned}
&\kappa_{23}\kappa_{34}(h_2+h_3+h_4)+\\
&+\kappa_{24}\kappa_{32}(h_2+h_3+h_4)+\\
&+\kappa_{24}\kappa_{34}(h_2+h_3+h_4)+\\
&+\kappa_{21}\kappa_{34}(h_3+h_4)+\\
&+\kappa_{21}\kappa_{32}h_4
\end{aligned}$$

on the right hand side.

Note that for a vertex $j \in \mathcal{C}''$ and a set $U \subseteq \mathcal{C}''$ there exists a $(\mathcal{C}' \cup \{j\})$-branching $\widetilde{\mathcal{R}}$ such that $V[\widetilde{\mathcal{R}}, j] = U$ if and only if

$$\text{for all } i' \in U \text{ there exists a } P \in \overrightarrow{i', j} \text{ such that } V[P] \subseteq U \text{ and} \tag{6.25}$$

$$\text{for all } i' \in \mathcal{C}''\backslash U \text{ there exists a } P \in \overrightarrow{i', \mathcal{C}'} \text{ such that } V[P] \subseteq \mathcal{C}\backslash U. \tag{6.26}$$

Let us define the set $\mathcal{C}''_{j-\mathrm{inarb}}$ by

$$\mathcal{C}''_{j-\mathrm{inarb}} = \{U \subseteq \mathcal{C}'' \mid U \text{ satisfies (6.25) and (6.26)}\}. \tag{6.27}$$

With this, we have

$$\vartheta_j = -\frac{1}{L_{\mathcal{D}}(\kappa)} \sum_{U \in \mathcal{C}''_{j-\mathrm{inarb}}} \left(h(U) \sum_{\substack{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}' \cup \{j\}) \\ V[\widetilde{\mathcal{R}}, j] = U}} \kappa_{\widetilde{\mathcal{R}}} \right).$$

Corollary 6.16 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network for which $\ell = t = 1$ and $\delta = 1$. Assume that $(\mathcal{C}, \mathcal{R})$ is not strongly connected and let $h \in \mathbb{R}^c$ be as in (6.1). Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$ if and only if*

$$\text{for all } j \in \mathcal{C}'' \text{ and} \begin{cases} \text{for all } U \in \mathcal{C}''_{j-\mathrm{inarb}} \text{ we have } h(U) \leq 0 \text{ and} \\ \text{there exists a } U \in \mathcal{C}''_{j-\mathrm{inarb}} \text{ such that } h(U) < 0. \end{cases} \tag{6.28}$$

Proof Since $L_{\mathcal{D}}(\kappa)$ is a positive number, it suffices to show that (6.28) is equivalent to

$$\text{for all } \kappa : \mathcal{R} \to \mathbb{R}_+ \text{ and for all } j \in \mathcal{C}'' \text{ we have } \sum_{U \in \mathcal{C}''_{j-\mathrm{inarb}}} \left(h(U) \sum_{\substack{\widetilde{\mathcal{R}} \in \mathcal{T}_{\mathcal{D}}(\mathcal{C}' \cup \{j\}) \\ V[\widetilde{\mathcal{R}}, j] = U}} \kappa_{\widetilde{\mathcal{R}}} \right) < 0. \tag{6.29}$$

It is obvious that (6.28) implies (6.29).

To prove the other direction, assume that (6.29) holds and fix $j \in \mathcal{C}''$. It is clear that the case $h(U) = 0$ for all $U \in \mathcal{C}''_{j-\mathrm{inarb}}$ would contradict (6.29). Thus, it suffices to exclude that there exists a $U \in \mathcal{C}''_{j-\mathrm{inarb}}$ such that $h(U) > 0$. Suppose by contradiction that $\overline{U} \in \mathcal{C}''_{j-\mathrm{inarb}}$ is such that

$h(\overline{U}) > 0$. If there is no other element of $\mathcal{C}''_{j-\text{inarb}}$ than $\overline{U}$ then we obviously get a contradiction with (6.29). So suppose for the rest of this proof that $\overline{U}$ is not the only element of $\mathcal{C}''_{j-\text{inarb}}$. Then

$$\sum_{U\in\mathcal{C}''_{j-\text{inarb}}}\left(h(U)\sum_{\substack{\widetilde{\mathcal{R}}\in\mathcal{T}_{\mathcal{D}}(\mathcal{C}'\cup\{j\})\\ V[\widetilde{\mathcal{R}},j]=U}}\kappa_{\widetilde{\mathcal{R}}}\right) = h(\overline{U})\sum_{\substack{\widetilde{\mathcal{R}}\in\mathcal{T}_{\mathcal{D}}(\mathcal{C}'\cup\{j\})\\ V[\widetilde{\mathcal{R}},j]=\overline{U}}}\kappa_{\widetilde{\mathcal{R}}} + \sum_{\substack{U\in\mathcal{C}''_{j-\text{inarb}}\\ U\neq\overline{U}}}\left(h(U)\sum_{\substack{\widetilde{\mathcal{R}}\in\mathcal{T}_{\mathcal{D}}(\mathcal{C}'\cup\{j\})\\ V[\widetilde{\mathcal{R}},j]=U}}\kappa_{\widetilde{\mathcal{R}}}\right), \tag{6.30}$$

where the first term on the right hand side is positive and is not affected by $\kappa|_{\varrho^{\text{in}}(\overline{U})\cup\varrho^{\text{out}}(\overline{U})}$, while for all $U\in\mathcal{C}''_{j-\text{inarb}}\backslash\{\overline{U}\}$ and for all $\widetilde{\mathcal{R}}\in\mathcal{T}_{\mathcal{D}}(\mathcal{C}'\cup\{j\})$ such that $V[\widetilde{\mathcal{R}},j]=U$, we have $\widetilde{\mathcal{R}}\cap(\varrho^{\text{in}}(\overline{U})\cup\varrho^{\text{out}}(\overline{U}))\neq\emptyset$. Thus, by setting the values of $\kappa|_{\varrho^{\text{in}}(\overline{U})\cup\varrho^{\text{out}}(\overline{U})}$ close enough to zero, we can achieve that the absolute value of the second term of the right hand side of (6.30) is smaller than the (positive) value of the first term in the same. This contradicts (6.29). $\square$

Note that Corollary 6.16 is a generalisation of Corollary 6.9. However, there are certain redundancies in the set of conditions in (6.28), and therefore our aim in the rest of this section is to get rid of these. In order to illustrate the result of Corollary 6.16 and also the redundancy in (6.28), consider that the graph of complexes takes the form

$$\begin{tikzcd}
 & & C_4 \arrow[r, shift left] & C_3 \arrow[l, shift left] \arrow[dr] & & \\
C_8 \arrow[r, shift left] & C_7 \arrow[l, shift left] \arrow[ur] \arrow[dr] & & & C_2 \arrow[r] & C_1. \\
 & & C_6 \arrow[r, shift left] \arrow[urr] & C_5 \arrow[l, shift left] \arrow[ur] & &
\end{tikzcd} \tag{6.31}$$

One can check by a short calculation that

$$\begin{array}{rcllllll}
\mathcal{C}''_{2-\text{inarb}} &=& \{ & \{2,3,4,5,6,7,8\} & & & & \}, \\
\mathcal{C}''_{3-\text{inarb}} &=& \{ & \{3,4\}, & \{3,4,7,8\} & & & \}, \\
\mathcal{C}''_{4-\text{inarb}} &=& \{ & \{4\}, & \{3,4\}, & \{4,7,8\}, & \{3,4,7,8\} & \}, \\
\mathcal{C}''_{5-\text{inarb}} &=& \{ & \{5\}, & \{5,6\}, & \{5,6,7,8\} & & \}, \\
\mathcal{C}''_{6-\text{inarb}} &=& \{ & \{6\}, & \{5,6\}, & \{6,7,8\}, & \{5,6,7,8\} & \}, \\
\mathcal{C}''_{7-\text{inarb}} &=& \{ & \{7,8\} & & & & \}, \text{ and} \\
\mathcal{C}''_{8-\text{inarb}} &=& \{ & \{8\}, & \{7,8\} & & & \}.
\end{array} \tag{6.32}$$

Note however that e.g. the set $\{3,4,7,8\}\in\mathcal{C}''_{3-\text{inarb}}$ is the disjoint union of the sets $\{3,4\}\in\mathcal{C}''_{3-\text{inarb}}$ and $\{7,8\}\in\mathcal{C}''_{7-\text{inarb}}$. Hence, once we require that $h(\{3,4\})\le 0$ and $h(\{7,8\})\le 0$, it is unnecessary to require also $h(\{3,4,7,8\})\le 0$, because then it is automatically satisfied. Similarly, one can easily see for (6.31) that for all $j\in\mathcal{C}''$ and for all $U\in\mathcal{C}''_{j-\text{inarb}}$, the set U is the disjoint union of some of the sets

$$\{2,3,4,5,6,7,8\}, \{3,4\}, \{4\}, \{5\}, \{6\}, \{7,8\}, \text{ and } \{8\}.$$

Moreover, such a partition of U is unique. Thus, for (6.31) the following are equivalent.

For all $j \in \mathcal{C}''$ and for all $U \in \mathcal{C}''_{j-\mathrm{inarb}}$ we have $h(U) \leq 0$.

We have $h(\{2,3,4,5,6,7,8\}) \leq 0$, $h(\{3,4\}) \leq 0$, $h(\{4\}) \leq 0$,
$h(\{5\}) \leq 0$, $h(\{6\}) \leq 0$, $h(\{7,8\}) \leq 0$, and $h(\{8\}) \leq 0$
(i.e., we require the non-positivity of h only for the first sets in each row of (6.32)).

We formulate in the following lemma that the above mentioned facts about (6.31) hold generally.

Lemma 6.17 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10). *For* $j \in \mathcal{C}''$ *let* $\mathcal{C}''_{j-\mathrm{inarb}}$ *be as in* (6.27). *For* $i \in \mathcal{C}$ *let us define* $U(i) \subseteq \mathcal{C}$ *by*

$$U(i) = \{k \in \mathcal{C} \mid \text{for all } P \in \overrightarrow{k, \mathcal{C}'} \text{ we have } i \in V[P]\}, \tag{6.33}$$

i.e., $k \in \mathcal{C}$ *is an element of* $U(i)$ *if all the directed paths from* k *to* $\mathcal{C}'$ *must traverse* i *(clearly, for* $i \in \mathcal{C}''$ *we have* $U(i) \subseteq \mathcal{C}''$*). Then*

(a) for all $j \in \mathcal{C}''$ *we have* $U(j) \in \mathcal{C}''_{j-\mathrm{inarb}}$ *and*

(b) for all $j \in \mathcal{C}''$ *and for all* $U \in \mathcal{C}''_{j-\mathrm{inarb}}$ *there exists a unique* $\mathcal{I}_U \subseteq \mathcal{C}''$ *such that*

$$U = \bigcup_{i \in \mathcal{I}_U}^{*} U(i),$$

where the symbol * *stresses that if* $i, i' \in \mathcal{I}_U$ *and* $i \neq i'$ *then* $U(i) \cap U(i') = \emptyset$.

The proof of Lemma 6.17 is carried out right after the proof of Lemma 6.18 below. Clearly, we have $U(\mathcal{C}') = \mathcal{C}$, but we will use the set $U(\mathcal{C}')$ only after Theorem 6.28. Before that, we will be interested in the collection $\{U(i) \mid i \in \mathcal{C}''\}$. We remark that the notation $U(i)$ is in accordance with the similar one in Subsection 6.1.2. Note that for the reaction network (6.31) we have

$$U(2) = \{2,3,4,5,6,7,8\}, U(3) = \{3,4\}, U(4) = \{4\}, U(5) = \{5\},$$
$$U(6) = \{6\}, U(7) = \{7,8\}, \text{ and } U(8) = \{8\}.$$

Before we prove Lemma 6.17, we explore some properties of the collection $\{U(i) \mid i \in \mathcal{C}''\}$ in the following lemma. Note that for all $k \in \mathcal{C}''$ there exists a directed path from k to $\mathcal{C}'$ (i.e., for all $k \in \mathcal{C}''$ we have $\overrightarrow{k, \mathcal{C}'} \neq \emptyset$).

Lemma 6.18 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10). *Let* $i, i' \in \mathcal{C}''$ *and define* $U(i)$ *and* $U(i')$ *as in* (6.33). *Then*

(a) $i \in U(i)$,

(b) if $i' \in U(i) \backslash \{i\}$ *then* $U(i') \subseteq U(i) \backslash \{i\}$,

(c) if $i \neq i'$ *then either* $U(i) \subsetneq U(i')$ *or* $U(i) \supsetneq U(i')$ *or* $U(i) \cap U(i') = \emptyset$, *and*

(d) $\varrho^{\text{out}}(U(i)) \subseteq \varrho^{\text{out}}(i)$ *(i.e., all the arcs that leave* $U(i)$ *have tail* i*).*

Proof Statement (a) is trivial.

To prove statement (b), assume that $i' \in U(i)\backslash\{i\}$ and let $i'' \in U(i')$. Then all the directed paths from i'' to $\mathcal{C}'$ traverse i' and since $i' \in U(i)$, they must also traverse i. This proves that $U(i') \subseteq U(i)$. To prove (b), it remains to show that $i \notin U(i')$. However, it is also obvious, because $i' \in U(i)$ guarantees that there exists a directed path from i' to $\mathcal{C}'$, which traverses i. Since there cannot be vertex repetition in a directed path and $i \neq i'$, this also shows that there exists a directed path from i to $\mathcal{C}'$ that does not traverse i'.

To show (c), suppose that $U(i) \cap U(i') \neq \emptyset$ and let $i'' \in U(i) \cap U(i')$. Then all the directed paths from i'' to $\mathcal{C}'$ must traverse both i and i'. Note that the order of i and i' on these directed paths must be the same, otherwise we could easily construct two directed paths from i'' to $\mathcal{C}'$, one of which avoids i and the other one avoids i'. As a consequence, either $i \in U(i')\backslash\{i'\}$ or $i' \in U(i)\backslash\{i\}$. In both cases we are done by (b).

To prove (d), suppose by contradiction that there exist $i' \in U(i)\backslash\{i\}$ and $i'' \in \mathcal{C}\backslash U(i)$ such that $(i', i'') \in \mathcal{R}$. Then there exists a $P \in \overrightarrow{i'', \mathcal{C}'}$ such that $i \notin V[P]$. Therefore $\text{con}(i', P) \in \overrightarrow{i', \mathcal{C}'}$ is a directed path that avoids i, contradicting $i' \in U(i)$ (see Appendix A for the definition of the concatenation). $\square$

Proof of Lemma 6.17 To prove (a), fix $j \in \mathcal{C}''$ and let $i' \in \mathcal{C}''$. Assume first that $i' \in U(j)$ and let $P \in \overrightarrow{i', \mathcal{C}'}$. By Lemma 6.18 (d), $V[P^{i':j}] \subseteq U(j)$ ($P^{i':j}$ denotes the part of P from i' to j, see Appendix A). Assume now that $i' \in \mathcal{C}''\backslash U(j)$. We need to show that there exists a directed path from i' to $\mathcal{C}'$ that avoids $U(j)$. Suppose by contradiction that for all $P \in \overrightarrow{i', \mathcal{C}'}$ we have $V[P] \cap U(j) \neq \emptyset$. Then, by Lemma 6.18 (d), it follows that $j \in V[P]$, which contradicts $i' \notin U(j)$.

It is left to prove (b). Fix $j \in \mathcal{C}''$ and $U \in \mathcal{C}''_{j-\text{inarb}}$. For $i \in U$, we have $U(i) \subseteq U$, because otherwise there would be an element $i' \in U(i)\backslash U$, for which there does not exist a directed path from i' to $\mathcal{C}'$, which avoids U. Since we also have $i \in U(i)$ (see Lemma 6.18 (a)), it holds that $U = \cup_{i \in U} U(i)$. From this and Lemma 6.18 (c) it follows that U is indeed the disjoint union of some $U(i)$'s and this partition is unique. Namely, those $U(i)$'s take part in the partition, which are maximal inside U. $\square$

We obtain the following corollary, which is the first step towards the simplification of (6.28).

Corollary 6.19 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10) *and let* $h \in \mathbb{R}^c$ *be arbitrary. For* $i, j \in \mathcal{C}''$ *let* $\mathcal{C}''_{j-\text{inarb}}$ *be as in* (6.27) *and let* $U(i)$ *be as in* (6.33)*. Then the following two statements are equivalent.*

(A) For all $j \in \mathcal{C}''$ *and for all* $U \in \mathcal{C}''_{j-\text{inarb}}$ *we have* $h(U) \leq 0$*.*

(B) For all $i \in \mathcal{C}''$ *we have* $h(U(i)) \leq 0$*.*

Proof Suppose that (A) holds. Then (B) directly follows from Lemma 6.17 (a).

Now suppose that (B) holds. Statement (A) is then obtained immediately from Lemma 6.17 (b). $\square$

Corollary 6.20 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network for which $\ell = t = 1$ and $\delta = 1$. Assume that $(\mathcal{C}, \mathcal{R})$ is not strongly connected and let $h \in \mathbb{R}^c$ be as in* (6.1)*. For $i, j \in \mathcal{C}''$ let $\mathcal{C}''_{j-\mathrm{inarb}}$ be as in* (6.27) *and let $U(i)$ be as in* (6.33)*. Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E^\kappa_+ \neq \emptyset$ if and only if*

$$\begin{cases} \textit{for all } i \in \mathcal{C}'' \textit{ we have } h(U(i)) \leq 0 \textit{ and} \\ \textit{for all } j \in \mathcal{C}'' \textit{ there exists an } i \in \cup_{U \in \mathcal{C}''_{j-\mathrm{inarb}}} \mathcal{I}_U \textit{ such that } h(U(i)) < 0, \end{cases} \tag{6.34}$$

where $\mathcal{I}_U$ is the unique subset of $\mathcal{C}''$ such that $U = \cup^*_{i' \in \mathcal{I}_U} U(i')$ (see Lemma 6.17 (b)).

Proof The equivalence is a direct consequence of Corollary 6.16, Lemma 6.17 (b), and Corollary 6.19. $\square$

In order to ease the notation in (6.34), we define for $j \in \mathcal{C}''$ the set $W(j)$ by

$$W(j) = \bigcup_{U \in \mathcal{C}''_{j-\mathrm{inarb}}} \mathcal{I}_U. \tag{6.35}$$

By Lemmas 6.17 (b) and 6.18 (c), for $i, j \in \mathcal{C}''$ and $U \in \mathcal{C}''_{j-\mathrm{inarb}}$ we have

$$i \in \mathcal{I}_U \text{ if and only if } i \in U \text{ and there does not exist } i' \in U \backslash \{i\} \text{ such that } i \in U(i'). \tag{6.36}$$

To illustrate the result of Corollary 6.20, note that for the reaction network (6.31) we have

$\{2, 3, 4, 5, 6, 7, 8\} = U(2)$,

$\{3, 4\} = U(3), \{3, 4, 7, 8\} = U(3) \cup^* U(7)$,

$\{4\} = U(4), \{3, 4\} = U(3), \{4, 7, 8\} = U(4) \cup^* U(7), \{3, 4, 7, 8\} = U(3) \cup^* U(7)$,

$\{5\} = U(5), \{5, 6\} = U(5) \cup^* U(6), \{5, 6, 7, 8\} = U(5) \cup^* U(6) \cup^* U(7)$,

$\{6\} = U(6), \{5, 6\} = U(5) \cup^* U(6), \{6, 7, 8\} = U(6) \cup^* U(7), \{5, 6, 7, 8\} = U(5) \cup^* U(6) \cup^* U(7)$,

$\{7, 8\} = U(7)$, and

$\{8\} = U(8), \{7, 8\} = U(7)$.

Thus,

$$\begin{array}{llll}
\mathcal{I}_{\{2,3,4,5,6,7,8\}} = \{2\}, & & & \\
\mathcal{I}_{\{3,4\}} = \{3\}, & \mathcal{I}_{\{3,4,7,8\}} = \{3, 7\}, & & \\
\mathcal{I}_{\{4\}} = \{4\}, & \mathcal{I}_{\{3,4\}} = \{3\}, & \mathcal{I}_{\{4,7,8\}} = \{4, 7\}, & \mathcal{I}_{\{3,4,7,8\}} = \{3, 7\}, \\
\mathcal{I}_{\{5\}} = \{5\}, & \mathcal{I}_{\{5,6\}} = \{5, 6\}, & \mathcal{I}_{\{5,6,7,8\}} = \{5, 6, 7\}, & \\
\mathcal{I}_{\{6\}} = \{6\}, & \mathcal{I}_{\{5,6\}} = \{5, 6\}, & \mathcal{I}_{\{6,7,8\}} = \{6, 7\}, & \mathcal{I}_{\{5,6,7,8\}} = \{5, 6, 7\}, \\
\mathcal{I}_{\{7,8\}} = \{7\}, \text{ and} & & & \\
\mathcal{I}_{\{8\}} = \{8\}, & \mathcal{I}_{\{7,8\}} = \{7\}, & &
\end{array}$$

and therefore

$$
\begin{aligned}
&W(2)=\{2\}, W(3)=\{3,7\}, W(4)=\{3,4,7\}, W(5)=\{5,6,7\}, \\
&W(6)=\{5,6,7\}, W(7)=\{7\}, \text{ and } W(8)=\{7,8\}.
\end{aligned} \tag{6.37}
$$

Since

$$W(7) \subseteq W(3), W(7) \subseteq W(4), W(7) \subseteq W(5), W(7) \subseteq W(6), \text{ and } W(7) \subseteq W(8),$$

once we require that there exist $i_2 \in W(2)$ and $i_7 \in W(7)$ such that $h(U(i_2)) < 0$ and $h(U(i_7)) < 0$ hold, it is unnecessary to require also e.g. that there exists an $i_4 \in W(4)$ such that $h(U(i_4)) < 0$, because that is automatically satisfied. Our aim is to get rid of these sort of redundancies in Corollary 6.20. For this, we first provide an equivalent description of $W(j)$ (recall that $(W(j)$ was defined in (6.35)) in Proposition 6.22. During the proof of that proposition, we will use the following corollary of Menger's Theorem.

Theorem 6.21 *Let $D = (V, A)$ be a directed graph and let s, t be such that $(s, t) \notin A$. Then there exist $P_1, P_2 \in \overrightarrow{s,t}$ such that $V[P_1] \cap V[P_2] = \{s, t\}$ if and only if for all $i \in V \backslash \{s, t\}$ there exists a $P \in \overrightarrow{s,t}$ such that $i \notin V[P]$.*

Proof The result is a direct consequence of Theorem A.1. See [51, Section 9.1] for more on Menger's Theorem. □

Proposition 6.22 *Assume that $(\mathcal{C}, \mathcal{R})$ satisfies* (6.10). *Let $j \in \mathcal{C}''$ and let $W(j)$ be as in* (6.35). *Then*

$$W(j) = \{i \in \mathcal{C}'' \mid \textit{there exist } P_j \in \overrightarrow{i,j} \textit{ and } P_{\mathcal{C}'} \in \overrightarrow{i,\mathcal{C}'} \textit{ such that } V[P_j] \cap V[P_{\mathcal{C}'}] = \{i\}\}. \tag{6.38}$$

Proof Denote by $Q(j)$ the set on the right hand side of (6.38). We will show (6.38) by showing that both $W(j) \subseteq Q(j)$ and $W(j) \supseteq Q(j)$ hold.

First we prove that $W(j) \subseteq Q(j)$ holds. By (6.35) and (6.36), we obtain for $i \in \mathcal{C}''$ that $i \in W(j)$ if and only if

$$\text{there exists a } U \in \mathcal{C}''_{j-\text{inarb}} \text{ such that } i \in U \text{ and for all } i' \in U \backslash \{i\} \text{ we have } i \notin U(i'). \tag{6.39}$$

To obtain an equivalent description of $Q(j)$, we will apply Theorem 6.21 for the directed graph

$$\widehat{\mathcal{D}} = (\mathcal{C} \cup \{\mathfrak{c}\}, \mathcal{R} \cup \{(j, \mathfrak{c}), (\mathcal{C}', \mathfrak{c})\}),$$

where $\mathfrak{c}$ is an auxiliary vertex. Thus, we have added the arcs $(j, \mathfrak{c})$ and $(\mathcal{C}', \mathfrak{c})$ to $\mathcal{R}$. Application of Theorem 6.21 with $s = i \in \mathcal{C}'' \backslash \{j\}$ and $t = \mathfrak{c}$ yields that for $i \in \mathcal{C}'' \backslash \{j\}$ we have $i \in Q(j)$ if and only if

$$\overrightarrow{i,j} \neq \emptyset \text{ and for all } i' \in \mathcal{C}'' \backslash \{i\} \text{ we have } i \notin U(i') \text{ or there exists a } P \in \overrightarrow{i,j} \text{ such that } i' \notin V[P], \tag{6.40}$$

where the "or" is inclusive. Using (6.25), it is obvious that (6.39) implies (6.40) for $i \in \mathcal{C}''\backslash\{j\}$. Thus, taking also into account that $j \in Q(j)$ holds obviously, we obtain the inclusion $W(j) \subseteq Q(j)$.

It is left to prove $W(j) \supseteq Q(j)$. Fix $i \in Q(j)$, $P_j \in \overrightarrow{i,j}$, and $P_{\mathcal{C}'} \in \overrightarrow{i,\mathcal{C}'}$ such that $V[P_j] \cap V[P_{\mathcal{C}'}] = \{i\}$. Let

$$U = \{i' \in \mathcal{C}'' \mid \text{there exists a } P \in \overrightarrow{i',j} \text{ such that } V[P] \cap V[P_{\mathcal{C}'}] \subseteq \{i\}\}, \tag{6.41}$$

i.e., we collect those vertices, from which it is possible to reach j without traversing $P_{\mathcal{C}'}$ except maybe in i. It is trivial that U in (6.41) satisfies (6.25). Also, it is easy to see that U in (6.41) fulfills (6.26). Thus, we have $U \in \mathcal{C}''_{j-\text{inarb}}$. The only thing it is left to check is that $i \in \mathcal{I}_U$. Clearly, $i \in U$ and $(V[P_{\mathcal{C}'}]\backslash\{i\}) \cap U = \emptyset$. Hence, there does not exist $i' \in U\backslash\{i\}$ such that $i \in U(i')$. Thus, by (6.36), we obtain that $i \in \mathcal{I}_U$. This concludes the proof of the inclusion $W(j) \supseteq Q(j)$. □

In case $j_1, j_2 \in \mathcal{C}''$ are such that $W(j_1) \subseteq W(j_2)$, it is redundant in Corollary 6.20 to require that there exists an $i \in W(j_2)$ such that $h(U(i)) < 0$, because this already follows if we require the same for j_1 instead of j_2. In order to get rid of these kind of redundancies, we take a closer look at the collection $\{W(j) \mid j \in \mathcal{C}''\}$. The following lemma is the key.

Lemma 6.23 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10). *For* $j \in \mathcal{C}''$ *let* $W(j)$ *be as in* (6.35). *Fix* $j_1, j_2 \in \mathcal{C}''$ *such that* $j_1 \in W(j_2)$. *Then* $W(j_1) \subseteq W(j_2)$.

Proof Let $j_3 \in W(j_1)$. Our aim is to show that j_3 is also an element of $W(j_2)$. If $j_3 = j_2$ then $j_3 \in W(j_2)$ trivially holds, so let us assume for the rest of this proof that $j_3 \neq j_2$. Similarly to the proof of Proposition 6.22, we will apply Theorem 6.21 to the directed graph

$$\widehat{\mathcal{D}} = (\mathcal{C} \cup \{\mathfrak{c}\}, \mathcal{R} \cup \{(j_2, \mathfrak{c}), (\mathcal{C}', \mathfrak{c})\}),$$

where $\mathfrak{c}$ is an auxiliary vertex. Let

$$P_{j_2} \in \overrightarrow{j_1, j_2} \text{ and } P_{\mathcal{C}'} \in \overrightarrow{j_1, \mathcal{C}'} \text{ be such that } V[P_{j_2}] \cap V[P_{\mathcal{C}'}] = \{j_1\} \text{ and}$$
$$Q_{j_1} \in \overrightarrow{j_3, j_1} \text{ and } Q_{\mathcal{C}'} \in \overrightarrow{j_3, \mathcal{C}'} \text{ be such that } V[Q_{j_1}] \cap V[Q_{\mathcal{C}'}] = \{j_3\}.$$

Clearly, once we show that for all $i \in \mathcal{C}\backslash\{j_3\}$ there exists a directed path from j_3 to $\mathfrak{c}$ in $\widehat{\mathcal{D}}$ that does not traverse i, we can draw the conclusion $j_3 \in W(j_2)$ by Theorem 6.21 and Proposition 6.22.

First let $i \in \mathcal{C}\backslash V[Q_{\mathcal{C}'}]$. Then $\mathrm{con}(Q_{\mathcal{C}'}, \mathfrak{c})$ is a directed path from j_3 to $\mathfrak{c}$ in $\widehat{\mathcal{D}}$ that does not traverse i.

It is left to treat the case $i \in V[Q_{\mathcal{C}'}]\backslash\{j_3\}$. Then $i \notin V[P_{j_2}]$ or $i \notin V[P_{\mathcal{C}'}]$, where the "or" is inclusive. If $i \notin V[P_{j_2}]$ then $\mathrm{con}(Q_{j_1}, P_{j_2}, \mathfrak{c})$ is a directed walk from j_3 to $\mathfrak{c}$ in $\widehat{\mathcal{D}}$ that does not traverse i. If $i \notin V[P_{\mathcal{C}'}]$ then $\mathrm{con}(Q_{j_1}, P_{\mathcal{C}'}, \mathfrak{c})$ is a directed walk from j_3 to $\mathfrak{c}$ in $\widehat{\mathcal{D}}$ that does not traverse i. In both cases, one can easily construct the desired directed path from the directed walk. □

For $j \in \mathcal{C}''$, denote by $\mathcal{C}''(j)$ the vertex set of that strong component of $(\mathcal{C}, \mathcal{R})$, which contains j. Thus, for (6.31) we have

$$\mathcal{C}''(2) = \{2\}, \mathcal{C}''(3) = \mathcal{C}''(4) = \{3, 4\}, \mathcal{C}''(5) = \mathcal{C}''(6) = \{5, 6\}, \text{ and } \mathcal{C}''(7) = \mathcal{C}''(8) = \{7, 8\}.$$

For $j \in \mathcal{C}''$ we say that it is possible to leave $\mathcal{C}''(j)$ through j if $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$. For (6.31), this property holds with $j \in \{2, 3, 5, 6, 7\}$.

Corollary 6.24 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10)*. For* $j \in \mathcal{C}''$ *let* $W(j)$ *be as in* (6.35)*. Let* $j \in \mathcal{C}''$ *be such that "it is possible to leave* $\mathcal{C}''(j)$ *through* j*" (i.e.,* $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$*). Then for all* $j' \in \mathcal{C}''(j)$ *we have* $W(j) \subseteq W(j')$*.*

Proof Fix $j' \in \mathcal{C}''(j)$. There exists a directed path from j to j' which uses only vertices in $\mathcal{C}''(j)$. On the other hand, since $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$, it is possible to reach $\mathcal{C}'$ from j using only vertices from $\mathcal{C} \backslash (\mathcal{C}''(j) \backslash \{j\})$. Hence, by Proposition 6.22, we have $j \in W(j')$. Lemma 6.23 concludes the proof. $\square$

It is clear from the above corollary that if $j_1, j_2 \in \mathcal{C}''$ are such that $\mathcal{C}''(j_1) = \mathcal{C}''(j_2)$, $\varrho^{\text{out}}(j_1) \cap \varrho^{\text{out}}(\mathcal{C}''(j_1)) \neq \emptyset$, and $\varrho^{\text{out}}(j_2) \cap \varrho^{\text{out}}(\mathcal{C}''(j_2)) \neq \emptyset$ then $W(j_1) = W(j_2)$. For the reaction network (6.31) we indeed have $W(5) = W(6)$.

Let $\mathcal{J}$ be a subset of $\mathcal{C}''$ for which

$$\begin{aligned}&\mathcal{J} \text{ contains precisely one element of each non-absorbing strong component of } (\mathcal{C}, \mathcal{R}) \text{ and}\\ &\text{for all } j \in \mathcal{J} \text{ we have } \varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset.\end{aligned} \tag{6.42}$$

For (6.31) we have two choices for $\mathcal{J}$. One is $\{2, 3, 5, 7\}$, while the other one is $\{2, 3, 6, 7\}$. To be concrete, let $\mathcal{J} = \{2, 3, 5, 7\}$. Due to Corollary 6.24, we have

$$W(3) \subseteq W(4), W(5) \subseteq W(6), \text{ and } W(7) \subseteq W(8),$$

which is indeed the case (see (6.37)).

We have thus obtained the following corollary.

Corollary 6.25 *Let* $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ *be a reaction network for which* $\ell = t = 1$ *and* $\delta = 1$*. Assume that* $(\mathcal{C}, \mathcal{R})$ *is not strongly connected and let* $h \in \mathbb{R}^c$ *be as in* (6.1)*. For* $i, j \in \mathcal{C}''$ *let* $U(i)$ *and* $W(j)$ *be as in* (6.33) *and* (6.35)*, respectively. Also, let* $\mathcal{J}$ *be as in* (6.42)*. Then for all* $\kappa : \mathcal{R} \to \mathbb{R}_+$ *we have* $E_+^\kappa \neq \emptyset$ *if and only if*

$$\begin{cases} \textit{for all } i \in \mathcal{C}'' \textit{ we have } h(U(i)) \leq 0 \textit{ and} \\ \textit{for all } j \in \mathcal{J} \textit{ there exists an } i \in W(j) \textit{ such that } h(U(i)) < 0. \end{cases}$$

Proof The equivalence directly follows from (6.35) and Corollaries 6.20 and 6.24. $\square$

Since for (6.31) we have made the choice $\mathcal{J} = \{2,3,5,7\}$, Corollary 6.25 suggests that the sets of importance are $W(2)$, $W(3)$, $W(5)$, and $W(7)$. Recall that

$$W(2) = \{2\}, W(3) = \{3,7\}, W(5) = \{5,6,7\}, \text{ and } W(7) = \{7\}. \tag{6.43}$$

As $7 \in W(3)$ and $7 \in W(5)$, by Lemma 6.23 we have $W(7) \subseteq W(3)$ and $W(7) \subseteq W(5)$ (which is anyway obvious from (6.43)). Thus, still there is redundancy in Corollary 6.25. Elimination of this redundancy is formulated in the following corollary.

Corollary 6.26 *Let $(\mathcal{X},\mathcal{C},\mathcal{R})$ be a reaction network for which $\ell = t = 1$ and $\delta = 1$. Assume that $(\mathcal{C},\mathcal{R})$ is not strongly connected and let $h \in \mathbb{R}^c$ be as in* (6.1)*. For $i,j \in \mathcal{C}''$ let $U(i)$ and $W(j)$ be as in* (6.33) *and* (6.35)*, respectively. Also, let $\mathcal{J}$ be as in* (6.42)*. Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E_+^\kappa \neq \emptyset$ if and only if*

$$\begin{cases} \text{for all } i \in \mathcal{C}'' \text{ we have } h(U(i)) \leq 0 \text{ and} \\ \text{for all } j \in \mathcal{J} \text{ with } W(j) \subseteq \mathcal{C}''(j), \text{ there exists an } i \in W(j) \text{ such that } h(U(i)) < 0. \end{cases} \tag{6.44}$$

Proof If $W(j) \not\subseteq \mathcal{C}''(j)$ for some $j \in \mathcal{J}$ then for $j' \in W(j) \backslash \mathcal{C}''(j)$ we have $W(j') \subseteq W(j)$ (see Lemma 6.23). Denote by j'' the sole element of the singleton $\mathcal{J} \cap \mathcal{C}''(j')$. Then we have $W(j'') \subseteq W(j') \subseteq W(j)$ (see Corollary 6.24). Hence, the statement "there exists an $i \in W(j'')$ such that $h(U(i)) < 0$" implies that "there exists an $i \in W(j)$ such that $h(U(i)) < 0$". Thus, the result follows from Corollary 6.25. □

For (6.31) we have

$$\begin{aligned} W(2) &= \{2\} \subseteq \{2\} = \mathcal{C}''(2), \\ W(3) &= \{3,7\} \not\subseteq \{3,4\} = \mathcal{C}''(3), \\ W(5) &= \{5,6,7\} \not\subseteq \{5,6\} = \mathcal{C}''(5), \text{ and} \\ W(7) &= \{7\} \subseteq \{7,8\} = \mathcal{C}''(7). \end{aligned} \tag{6.45}$$

To simplify further the condition (6.44), we examine in the following proposition the collection $\{U(i) \mid i \in W(j)\}$, where $j \in \mathcal{C}''$ is such that $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$ and $W(j) \subseteq \mathcal{C}''(j)$.

Lemma 6.27 *Assume that $(\mathcal{C},\mathcal{R})$ satisfies* (6.10)*. For $i,j \in \mathcal{C}''$ let $U(i)$ and $W(j)$ be as in* (6.33) *and* (6.35)*, respectively. Fix $j \in \mathcal{C}''$ such that $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$ and $W(j) \subseteq \mathcal{C}''(j)$. Then the sets $\{U(i) \mid i \in W(j)\}$ are disjoint and $\cup^*_{i \in W(j)} U(i) = U(\mathcal{C}''(j))$, where*

$$U(\mathcal{C}''(j)) = \{k \in \mathcal{C}'' \mid \textit{all directed paths from } k \textit{ to } \mathcal{C}' \textit{ traverse } \mathcal{C}''(j)\}. \tag{6.46}$$

Proof First we prove that the sets $\{U(i) \mid i \in W(j)\}$ are disjoint. Let $i_1, i_2 \in W(j)$ be such that $i_1 \neq i_2$. Due to Lemma 6.18 (c), it suffices to show that none of $U(i_1)$ and $U(i_2)$ contains the other one. Suppose by contradiction that $U(i_2) \subseteq U(i_1) \backslash \{i_1\}$. Let $P_j \in \overrightarrow{i_2, j}$ and $P_{\mathcal{C}'} \in \overrightarrow{i_2, \mathcal{C}'}$ be such that $V[P_j] \cap V[P_{\mathcal{C}'}] = \{i_2\}$ (see Proposition 6.22). Since $i_2 \in U(i_1)$ by our hypothesis ($i_2 \in U(i_2)$ by Lemma 6.18 (a)), we have $i_1 \in V[P_{\mathcal{C}'}]$. Since $i_1 \neq i_2$, we have $i_1 \notin V[P_j]$. Let

$P \in \overrightarrow{j, \mathcal{C}'}$ be such that $V[P] \cap \mathcal{C}''(j) = \{j\}$ (recall that $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$). Then clearly $i_1 \notin V[P]$ (recall that $i_1 \in W(j) \subseteq \mathcal{C}''(j)$ and the case $i_1 = j$ can trivially be excluded). Thus, $\text{con}(P_j, P) \in \overrightarrow{i_2, \mathcal{C}'}$ and $i_1 \notin V[\text{con}(P_j, P)]$, contradicting $i_2 \in U(i_1)$. This contradiction proves that the sets $\{U(i) \mid i \in W(j)\}$ are indeed disjoint.

It is left to prove that $\cup^*_{i \in W(j)} U(i) = U(\mathcal{C}''(j))$. It is obvious that $U(\mathcal{C}''(j)) \in \mathcal{C}''_{j-\text{inarb}}$ (one can prove this similarly to the proof Lemma 6.17 (a)). Hence, we have $\mathcal{I}_{U(\mathcal{C}''(j))} \subseteq W(j)$ (see (6.35)). Also, note that for $i \in W(j)$ we have $i \in \mathcal{C}''(j)$ (recall that have we assumed in the lemma that $W(j) \subseteq \mathcal{C}''(j)$). Thus, for $i \in W(j)$ we obviously have $U(i) \subseteq U(\mathcal{C}''(j))$. Therefore,

$$U(\mathcal{C}''(j)) = \bigcup^*_{i \in \mathcal{I}_{U(\mathcal{C}''(j))}} U(i) \subseteq \bigcup^*_{i \in W(j)} U(i) \subseteq U(\mathcal{C}''(j)).$$

As a consequence, all the inclusions in the above chain are equality. This concludes the proof of $\cup^*_{i \in W(j)} U(i) = U(\mathcal{C}''(j))$. $\square$

As a consequence, we obtain Theorem 6.28 below, which is the main result of this chapter. Recall that for $i, j \in \mathcal{C}''$

- $U(i) = \{k \in \mathcal{C}'' \mid$ all directed paths from k to $\mathcal{C}'$ traverse $i\}$,
- $\mathcal{C}''(j)$ denotes the vertex set of that strong component of $(\mathcal{C}, \mathcal{R})$ which contains j,
- $U(\mathcal{C}''(j)) = \{k \in \mathcal{C}'' \mid$ all directed paths from k to $\mathcal{C}'$ traverse $\mathcal{C}''(j)\}$, and
- $W(j) = \{k \in \mathcal{C}'' \mid$ there exist $P_j \in \overrightarrow{k, j}$ and $P_{\mathcal{C}'} \in \overrightarrow{k, \mathcal{C}'}$ such that $V[P_j] \cap V[P_{\mathcal{C}'}] = \{k\}\}$.

Also, recall that $\mathcal{J} \subseteq \mathcal{C}''$ is such that $\mathcal{J}$ contains precisely one element of each non-absorbing strong component of $(\mathcal{C}, \mathcal{R})$ and for all $j \in \mathcal{J}$ we have $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$.

Theorem 6.28 *Let $(\mathcal{X}, \mathcal{C}, \mathcal{R})$ be a reaction network for which $\ell = t = 1$ and $\delta = 1$. Assume that $(\mathcal{C}, \mathcal{R})$ is not strongly connected and let $h \in \mathbb{R}^c$ be as in* (6.1)*. For $i, j \in \mathcal{C}''$ let $U(i)$, $W(j)$, and $U(\mathcal{C}''(j))$ be as in* (6.33), (6.35), *and* (6.46), *respectively. Also, let $\mathcal{J}$ be as in* (6.42). *Then for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E^\kappa_+ \neq \emptyset$ if and only if*

$$\begin{cases} \text{for all } i \in \mathcal{C}'' \text{ we have } h(U(i)) \leq 0 \text{ and} \\ \text{for all } j \in \mathcal{J} \text{ with } W(j) \subseteq \mathcal{C}''(j), \text{ we have } h(U(\mathcal{C}''(j))) < 0. \end{cases}$$

Proof The statement directly follows from Corollary 6.26 and Lemma 6.27. $\square$

Since for (6.31) we have $U(\mathcal{C}''(2)) = U(2)$ and $U(\mathcal{C}''(7)) = U(7)$ we obtain that for all $\kappa : \mathcal{R} \to \mathbb{R}_+$ we have $E^\kappa_+ \neq \emptyset$ if and only if

$$h(\{2,3,4,5,6,7,8\}) < 0, h(\{3,4\}) \leq 0, h(\{4\}) \leq 0, h(\{5\}) \leq 0,$$
$$h(\{6\}) \leq 0, h(\{7,8\}) < 0, \text{ and } h(\{8\}) \leq 0.$$

Since the condition $W(j) \subseteq \mathcal{C}''(j)$ appeared in our main result, the rest of this section is devoted to provide an equivalent (and more transparent) condition to that. After some preparations, we will arrive to this equivalent condition in Proposition 6.30. Let us start by defining the set $\mathcal{U}(j)$ for $j \in \mathcal{J}$ by

$$\mathcal{U}(j) = \bigcup_{j' \in \mathcal{C}''(j)} U(j'). \tag{6.47}$$

Also, let $\mathcal{U}(\mathcal{C}') = U(\mathcal{C}')$ (thus, $\mathcal{U}(\mathcal{C}') = \mathcal{C}$). Note that for (6.31) we have

$$\mathcal{U}(2) = \{2, 3, 4, 5, 6, 7, 8\}, \mathcal{U}(3) = \{3, 4\}, \mathcal{U}(5) = \{5, 6\}, \text{ and } \mathcal{U}(7) = \{7, 8\}.$$

The following proposition states that the collection $\{\mathcal{U}(j) \mid j \in \mathcal{J}\}$ has a similar property as the collection $\{U(i) \mid i \in \mathcal{C}''\}$ has.

Proposition 6.29 *Assume that $(\mathcal{C}, \mathcal{R})$ satisfies (6.10). Let $\mathcal{J}$ be as in (6.42) and for $j \in \mathcal{J}$ let $\mathcal{U}(j)$ be as in (6.47). Let $j_1, j_2 \in \mathcal{J}$ be such that $j_1 \neq j_2$. Then either $\mathcal{U}(j_1) \subsetneq \mathcal{U}(j_2)$ or $\mathcal{U}(j_1) \supsetneq \mathcal{U}(j_2)$ or $\mathcal{U}(j_1) \cap \mathcal{U}(j_2) = \emptyset$.*

Proof Suppose that $\mathcal{U}(j_1) \cap \mathcal{U}(j_2) \neq \emptyset$. Let $j_1' \in \mathcal{C}''(j_1)$ and $j_2' \in \mathcal{C}''(j_2)$ be such that $U(j_1') \cap U(j_2') \neq \emptyset$. Then, by Lemma 6.18 (b) and (c), either $U(j_1') \subsetneq U(j_2') \backslash \{j_2'\}$ or $U(j_1') \backslash \{j_1'\} \supsetneq U(j_2')$. Clearly, the two cases are symmetric. Suppose for the rest of this proof that $U(j_1') \subsetneq U(j_2') \backslash \{j_2'\}$. Since j_1' and j_2' are not in the same strong component, this has the consequence that $\mathcal{C}''(j_1) \subsetneq U(j_2')$. Thus, by Lemma 6.18 (b), we have

$$\mathcal{U}(j_1) = \bigcup_{j' \in \mathcal{C}''(j_1)} U(j') \subseteq U(j_2') \backslash \{j_2'\} \subsetneq U(j_2') \subseteq \bigcup_{j' \in \mathcal{C}''(j_2)} U(j') = \mathcal{U}(j_2),$$

which concludes the proof. □

A collection $\mathcal{Q}$ of subsets of a set is called *laminar* if for all $Q_1, Q_2 \in \mathcal{Q}$ we have

$$Q_1 \subseteq Q_2 \text{ or } Q_1 \supseteq Q_2 \text{ or } Q_1 \cap Q_2 = \emptyset.$$

Thus, by Lemma 6.18 (c) and Proposition 6.29 both the collections

$$\{U(i) \mid i \in \mathcal{C}''\} \cup \{\mathcal{C}\} \text{ and } \{\mathcal{U}(j) \mid j \in \mathcal{J}\} \cup \{\mathcal{C}\} \tag{6.48}$$

are laminar. It is straightforward to associate a branching to a laminar collection $\mathcal{Q}$ that consists of distinct sets. The vertex set of the branching is $\mathcal{Q}$ itself, while for $Q_1, Q_2 \in \mathcal{Q}$ the ordered pair (Q_1, Q_2) is an arc if $Q_1 \subseteq Q_2$ and there does not exist $Q_3 \in \mathcal{Q}$ such that $Q_1 \subseteq Q_3 \subseteq Q_2$. Denote by T and $\mathcal{T}$ the arborescences associated to the laminar collections in (6.48), respectively (since all the other sets of these two collections are contained in $\mathcal{C}$, the associated branching is actually an arborescence with root $\mathcal{C}$). We have depicted T and $\mathcal{T}$ associated to (6.31) in Figure 6.2.

It is also straightforward to associate to a directed graph $D = (V, A)$ an acyclic directed graph, denoted by $\mathfrak{T}_D$, in the following way. Denote by $V^1, \ldots, V^k$ the vertex sets of the strong

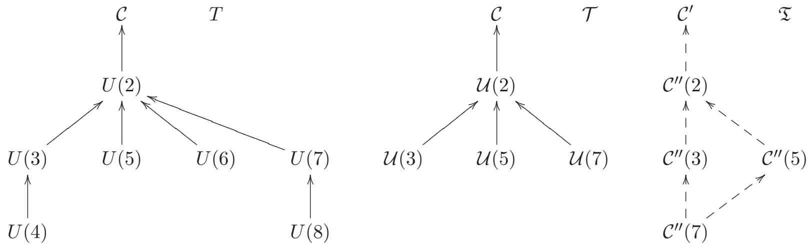


Figure 6.2: The arborescences T and $\mathcal{T}$ associated to the laminar families (6.48) and the acyclic directed graph $\mathfrak{T}$ for (6.31).

components of D. The vertex set of $\mathfrak{T}_D$ is then $\{V^1, \ldots, V^k\}$, while for $k_1, k_2 \in \{1, \ldots, k\}$ such that $k_1 \neq k_2$, the ordered pair (V^{k_1}, V^{k_2}) is an arc of $\mathfrak{T}_D$ if $\varrho_D^{\mathrm{out}}(V^{k_1}) \cap \varrho_D^{\mathrm{in}}(V^{k_2}) \neq \emptyset$. We will simply denote by $\mathfrak{T}$ the acyclic directed graph $\mathfrak{T}_{(\mathcal{C},\mathcal{R})}$. Thus, the vertex set of $\mathfrak{T}$ is $\{\mathcal{C}''(j) \mid j \in \mathcal{J}\} \cup \{\mathcal{C}'\}$. We have depicted $\mathfrak{T}$ associated to (6.31) in Figure 6.2.

For the sake of simplicity, we perform some natural identifications. We identify from this point on

$$\text{the vertex sets of } T,\ \mathcal{T}, \text{ and } \mathfrak{T} \text{ with the sets } \mathcal{C}'' \cup \{\mathcal{C}'\},\ \mathcal{J} \cup \{\mathcal{C}'\}, \text{ and } \mathcal{J} \cup \{\mathcal{C}'\},$$

respectively (recall that $U(\mathcal{C}') = \mathcal{C}$ and $\mathcal{U}(\mathcal{C}') = \mathcal{C}$). With these identifications, the arborescence $\mathcal{T}$ and the acyclic directed graph $\mathfrak{T}$ have the same vertex set, which makes it possible to depict them at once. We have depicted T, $\mathcal{T}$, and $\mathfrak{T}$ considering these identifications in Figure 6.3.

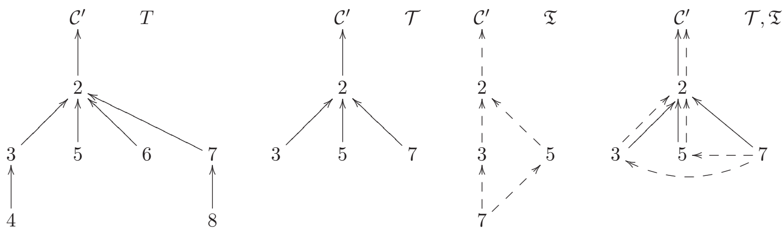


Figure 6.3: The arborescences T and $\mathcal{T}$ associated to the laminar families (6.48) and the acyclic directed graph $\mathfrak{T}$ for (6.31) considering the straightforward identifications of the vertex sets.

The following proposition states that for $j \in \mathcal{J}$ the condition $W(j) \subseteq \mathcal{C}''(j)$ can be expressed in terms of $\mathcal{T}$ and $\mathfrak{T}$. For a directed graph $D = (V, A)$ and $j \in V$ let us denote by $R_D(j)$ the set of vertices from which it is possible to reach j in D, i.e.,

$$R_D(j) = \{\widetilde{j} \in V \mid \text{there exists a directed path from } \widetilde{j} \text{ to } j \text{ in } D\}. \tag{6.49}$$

It is trivial that for all $j \in \mathcal{J}$ we have $R_{\mathcal{T}}(j) \subseteq R_{\mathfrak{T}}(j)$.

Proposition 6.30 *Assume that* $(\mathcal{C}, \mathcal{R})$ *satisfies* (6.10)*. Let* $\mathcal{J}$ *be as in* (6.42) *and for* $j \in \mathcal{C}''$ *let* $W(j)$ *be as in* (6.35)*. Also, let the arborescence* $\mathcal{T}$ *and acyclic directed graph* $\mathfrak{T}$ *be as above. Fix* $j \in \mathcal{J}$*. Then* $W(j) \subseteq \mathcal{C}''(j)$ *if and only if* $R_{\mathcal{T}}(j) = R_{\mathfrak{T}}(j)$*, where* $R_{\mathcal{T}}(j)$ *and* $R_{\mathfrak{T}}(j)$ *are understood in accordance with* (6.49)*.*

Proof Assume first that $R_{\mathcal{T}}(j) = R_{\mathfrak{T}}(j)$ and suppose by contradiction that $W(j)\backslash\mathcal{C}''(j) \neq \emptyset$. Let $i \in W(j)\backslash\mathcal{C}''(j)$, $P_j \in \overrightarrow{i,j}$, and $P_{\mathcal{C}'} \in \overrightarrow{i,\mathcal{C}'}$ be such that $V[P_j] \cap V[P_{\mathcal{C}'}] = \{i\}$ (see Proposition 6.22). Also, let $P \in \overrightarrow{j,\mathcal{C}'}$ be such that $V[P] \cap \mathcal{C}''(j) = \{j\}$ (recall that $\varrho^{\text{out}}(j) \cap \varrho^{\text{out}}(\mathcal{C}''(j)) \neq \emptyset$). Then both $P_{\mathcal{C}'}$ and $\text{con}(P_j, P)$ are directed paths from i to $\mathcal{C}'$ and these two cannot have any common vertex in $\mathcal{C}''(j)$. Thus, there does not exist $j' \in \mathcal{C}''(j)$ such that $i \in U(j')$, and consequently $i \notin \mathcal{U}(j)$. Let $\bar{j} \in \mathcal{J}$ be such that $i \in \mathcal{C}''(\bar{j})$. Then $\bar{j} \in R_{\mathfrak{T}}(j)$ and $\bar{j} \notin R_{\mathcal{T}}(j)$, which contradicts $R_{\mathcal{T}}(j) = R_{\mathfrak{T}}(j)$.

To show the other direction, assume that $W(j) \subseteq \mathcal{C}''(j)$ and suppose by contradiction that $i \in \mathcal{C}''$ is such that $\overrightarrow{i,j} \neq \emptyset$ and there does not exist $j' \in \mathcal{C}''(j)$ such that $i \in U(j')$. Moreover, assume that i is such that $\overrightarrow{p_T(i),j} = \emptyset$, where $p_T(i) \in \mathcal{C}$ is the *parent* of i in T (i.e., $p_T(i)$ is the second vertex on the unique directed path from i to $\mathcal{C}'$ in T). Since $i \in U(i)$, it follows that $i \notin \mathcal{C}''(j)$. We will show that $i \in W(j)$, which will thus contradict $W(j) \subseteq \mathcal{C}''(j)$. To show the inclusion $i \in W(j)$, note that the set $\{i' \in \mathcal{C}''\backslash\{i\} \mid i \in U(i')\}$ coincides with $V[P]\backslash\{i, \mathcal{C}'\}$, where P is the unique directed path from i to $\mathcal{C}'$ in T. However, by our assumption on i, for all $i' \in V[P]\backslash\{i, \mathcal{C}'\}$ we have $\overrightarrow{i',j} = \emptyset$. Thus, taking also into account Proposition 6.22 and (6.40) in the proof of that proposition, we obtain that $i \in W(j)$. This concludes the proof. $\square$

For the reaction network (6.31) we have

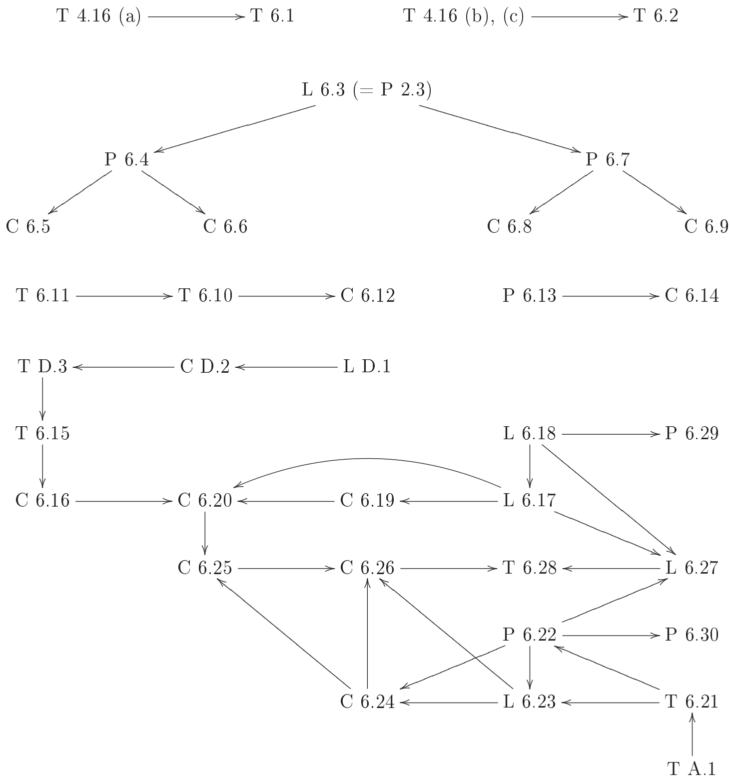
$$\begin{aligned}
R_{\mathcal{T}}(2) = \{2,3,5,7\} &= \{2,3,5,7\} = R_{\mathfrak{T}}(2),\\
R_{\mathcal{T}}(3) = \{3\} &\subsetneq \{3,7\} = R_{\mathfrak{T}}(3),\\
R_{\mathcal{T}}(5) = \{5\} &\subsetneq \{5,7\} = R_{\mathfrak{T}}(5), \text{ and}\\
R_{\mathcal{T}}(7) = \{7\} &= \{7\} = R_{\mathfrak{T}}(7),
\end{aligned}$$

which is indeed in accordance with (6.45).

We conclude this section by some remarks on the collection $\{U(i) \mid i \in \mathcal{C}''\} \cup \{\mathcal{C}\}$. First, note that not only $\{U(i) \mid i \in \mathcal{C}''\} \cup \{\mathcal{C}\}$ determines T, but also conversely. Indeed, it is obvious that $U(i) = R_T(i)$ for all $i \in \mathcal{C}$. In graph theory, if $j \in U(i)$ then we say that i *postdominates* j. The arborescence T is called the *postdominator tree*. See e.g. [35] for more on algorithmic issues concerning the dominator/postdominator tree.

6.4 The acyclic directed graph of the implications

We have depicted below the acyclic directed graph of the implications of this chapter. For the organising principle of this directed graph, see Section 2.8.



Appendix A

Directed graphs

We collect in this chapter those standard concepts and notations from graph theory that are used throughout this thesis. The notions are taken from [51, Sections 3.2, 9.1, and 10.1].

Let $D = (V, A)$ be a directed graph without multiple arcs throughout this section.

For $i_0, i_1, \ldots, i_l \in V$ with a nonnegative integer l, we say that $P = (i_0, i_1, \ldots, i_l)$ is a *directed walk from i_0 to i_l*, or just a *directed walk*, if $(i_k, i_{k+1}) \in A$ for all $k \in \{0, 1, \ldots, l-1\}$. The *length* of a directed walk $P = (i_0, i_1, \ldots, i_l)$, denoted by $\mathrm{len}(P)$, is l. For a directed walk $P = (i_0, i_1, \ldots, i_l)$, we denote by $V[P]$ the vertex set $\{i_0, i_1, \ldots, i_l\}$ (we use the notation $V[P]$ even if the vertex set of the directed graph in question is denoted by some other symbol than V). If $i \in V[P]$ for a directed walk P then we say that P *traverses* i, while if $i \notin V[P]$ then we say that P *avoids* i. One can define traversing and avoiding a set $U \subseteq V$ similarly. A directed walk $P = (i_0, i_1, \ldots, i_l)$ is said to be a *directed path* if $i_0, i_1, \ldots, i_l$ are all distinct. For $i, j \in V$, we denote by $\overrightarrow{i,j}$ the set of directed paths from i to j. For a directed path $P = (i_0, i_1, \ldots, i_l)$ and $0 \leq k \leq m \leq l$ we denote by $P^{i_k:i_m}$ the directed path $(i_k, i_{k+1}, \ldots, i_m)$. A directed walk $P = (i_0, i_1, \ldots, i_l)$ is said to be a *directed circuit* if $l \geq 1$, $i_0 = i_l$, and $i_0, i_1, \ldots, i_{l-1}$ are all distinct.

For the directed walks $P_1 = (i_0, i_1, \ldots, i_l)$ and $P_2 = (j_0, j_1, \ldots, j_k)$ with $i_l = j_0$, we denote by $\mathrm{con}(P_1, P_2)$ their *concatenation*, which is defined by $\mathrm{con}(P_1, P_2) = (i_0, \ldots, i_l, j_1, \ldots, j_k)$. Clearly, $\mathrm{con}(P_1, P_2)$ is then a directed walk from i_0 to j_k.

The directed graph D is called *strongly connected* if for all $i, j \in V$ we have $\overrightarrow{i,j} \neq \emptyset$, while it is called *weakly connected* if the underlying undirected graph is connected. The maximal strongly connected subgraphs of D are called the *strong components* of D, while the maximal weakly connected subgraphs of D are called the *weak components* of D. An *absorbing strong component* of D is a strong component such that there is no arc, which leaves it.

The above definitions are in accordance with the ones in [51, Section 3.2], with the only difference that we have defined a directed walk as a sequence of vertices rather than an alternating sequence of vertices and arcs. This choice is made here, because it suffices all our purposes in this thesis if we restrict our attention to directed graphs without multiple arcs.

We use a corollary of the following theorem several times in Section 6.3. See [51, Corollary 9.1a] for a proof of Menger's Theorem.

Theorem A.1 (Menger's Theorem [51]) *Let $D = (V, A)$ be a directed graph and let s and t be two nonadjacent vertices of D. Then the maximum number of internally vertex-disjoint $s - t$ paths is equal to the minimum size of an $s - t$ vertex-cut.*

For $U \subseteq V$, the set of arcs, which *enter* U and *leave* U are defined by

$$\varrho_D^{\text{in}}(U) = \{(i,j) \in A \mid i \in V \backslash U, j \in U\} \text{ and}$$
$$\varrho_D^{\text{out}}(U) = \{(i,j) \in A \mid i \in U, j \in V \backslash U\},$$

respectively. We simply write $\varrho^{\text{in}}(U)$ and $\varrho^{\text{out}}(U)$ instead of $\varrho_D^{\text{in}}(U)$ and $\varrho_D^{\text{out}}(U)$, respectively, if the directed graph in question is clearly determined by the context. Denote by 2^V the power set of V. For a function $z : A \to \mathbb{R}$, define the function $\text{excess}_z : 2^V \to \mathbb{R}$ by

$$\text{excess}_z(U) = z(\varrho^{\text{in}}(U)) - z(\varrho^{\text{out}}(U)) \quad (U \subseteq V),$$

where $z(\varrho^{\text{in}}(U))$ and $z(\varrho^{\text{out}}(U))$ are understood in accordance with (1.1). For $i \in V$ we use the notations $\varrho^{\text{in}}(i)$, $\varrho^{\text{out}}(i)$, and $\text{excess}_z(i)$ instead of $\varrho^{\text{in}}(\{i\})$, $\varrho^{\text{out}}(\{i\})$, and $\text{excess}_z(\{i\})$, respectively. Note that $\text{excess}_z(V) = \text{excess}_z(\emptyset) = 0$.

An important and frequently used observation is that

$$\text{excess}_z(U) = \sum_{i \in U} \text{excess}_z(i) \text{ for all } U \subseteq V. \tag{A.1}$$

Thus, the excess function satisfies (1.1).

For a function $h : V \to \mathbb{R}$, a function $z : A \to \mathbb{R}$ is called an *h-transshipment* if

$$\text{excess}_z(i) = h(i) \text{ for all } i \in V.$$

Let us define $\mathcal{A}_D(U)$ and $\mathcal{T}_D(U)$ by

$$\mathcal{A}_D(U) = \left\{ \widetilde{A} \subseteq A \;\middle|\; \begin{array}{l} |\varrho^{\text{out}}_{(V,\widetilde{A})}(k)| = 0 \text{ for all } k \in U \text{ and} \\ |\varrho^{\text{out}}_{(V,\widetilde{A})}(k)| = 1 \text{ for all } k \in V \backslash U \end{array} \right\} \text{ and}$$
$$\mathcal{T}_D(U) = \{\widetilde{A} \in \mathcal{A}_D(U) \mid (V, \widetilde{A}) \text{ is acyclic}\},$$

respectively. (A directed graph is called *acyclic* if it has no directed circuits.) The elements of $\mathcal{T}_D(U)$ are called *U-branchings in D* (or more precisely, *U-inbranchings in D*), the set U being called the *root set*. If U is the singleton $\{j\}$ for some $j \in V$ then a U-branching $\widetilde{A}$ is called a *j-arborescence* (or more precisely, a *j-inarborescence*). Clearly, if $U = \{j_1, \ldots, j_k\}$ for some positive integer k then for a U-branching $\widetilde{A}$, $(V, \widetilde{A})$ has k weak components, each of them is corresponding to an element of U. Denote these weak components by $(V^{j_1}, \widetilde{A}^{j_1}), \ldots, (V^{j_k}, \widetilde{A}^{j_k})$. Then $\widetilde{A}^j$ is a j-arborescence in the directed graph

$$(V^j, \{(i, i') \in A \mid i, i' \in V^j\})$$

for all $j \in U$. See Figure A.1 for an illustration of these notions.

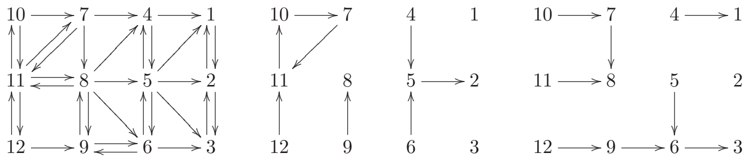


Figure A.1: A directed graph D with vertex set $\{1, \ldots, 12\}$ (on the left) and two elements of $\mathcal{A}_D(\{1,2,3,8\})$ (in the middle and on the right). The one in the middle is *not* acyclic, and hence, it does not belong to $\mathcal{T}_D(\{1,2,3,8\})$, while the one on the right is acyclic, so that one is a $\{1,2,3,8\}$-branching in D. It is also apparent that the latter one can be decomposed into four arborescences, the roots of these four arborescences are 1, 2, 3, and 8, respectively.

We also use the following notations in Section 6.3 and Section D.2. For $i, j \in V$ let us define $\mathcal{A}_D^{ij}(U)$ and $\mathcal{T}_D^{ij}(U)$ by

$$\mathcal{A}_D^{ij}(U) = \{\widetilde{A} \in \mathcal{A}_D(U) \mid \text{there exists a directed path from } i \text{ to } j \text{ in } (V, \widetilde{A})\} \text{ and} \tag{A.2}$$

$$\mathcal{T}_D^{ij}(U) = \{\widetilde{A} \in \mathcal{T}_D(U) \mid \text{there exists a directed path from } i \text{ to } j \text{ in } (V, \widetilde{A})\}, \tag{A.3}$$

respectively.

Appendix B

Linear algebra

We have collected in this chapter a few results from linear algebra. Corollary B.2 plays a crucial role in the proof Theorem 3.6, while Propositions B.3 and B.4 are used in Sections 2.6 and 2.7.

The first statement of this appendix is the well known Farkas' Lemma. We omit its proof.

Proposition B.1 *Let c and n be positive integers. Let $A \in \mathbb{R}^{c\times n}$ and $b \in \mathbb{R}^c$. Then*

$$\{x \in \mathbb{R}^n \mid Ax = b\} = \emptyset \textit{ if and only if } \{y \in \mathbb{R}^c \mid A^\top y = 0, b^\top y \neq 0\} \neq \emptyset.$$

For the linear subspaces $V_1, V_2, \ldots, V_k$ of a vector space V, the notation $V = V_1 \oplus V_2 \oplus \cdots \oplus V_k$ expresses that V is the direct sum of $V_1, V_2, \ldots, V_k$, i.e.,

(i) for all $v \in V$ there exists a $(v_1, v_2, \ldots, v_k) \in V_1 \times V_2 \times \cdots \times V_k$ such that $v = v_1 + v_2 + \cdots + v_k$ and

(ii) if $0 = v_1 + v_2 + \ldots + v_k$ for some $(v_1, v_2, \ldots, v_k) \in V_1 \times V_2 \times \cdots \times V_k$ then $v_1 = 0$, $v_2 = 0, \ldots, v_k = 0$.

A corollary of the above proposition is the following.

Corollary B.2 *Let ℓ, n, and $c^1, c^2, \ldots, c^\ell$ be positive integers. Let $A_r \in \mathbb{R}^{c^r\times n}$ and $b_r \in \mathbb{R}^{c^r}$ $(r \in \overline{1,\ell})$. Assume that*

(i) $\{x \in \mathbb{R}^n \mid A_r x = b_r\} \neq \emptyset$ *for all* $r \in \overline{1,\ell}$ *and*

(ii) $\operatorname{ran}[A_1^\top, A_2^\top, \ldots, A_\ell^\top] = \operatorname{ran} A_1^\top \oplus \operatorname{ran} A_2^\top \oplus \cdots \oplus \operatorname{ran} A_\ell^\top$.

Then

$$\bigcap_{r=1}^{\ell} \{x \in \mathbb{R}^n \mid A_r x = b_r\} \neq \emptyset.$$

Proof Suppose by contradiction that $\cap_{r=1}^{\ell}\{x \in \mathbb{R}^n \mid A_r x = b_r\} = \emptyset$. Then, by Proposition B.1, there exist $y_r \in \mathbb{R}^{c^r}$ $(r \in \overline{1,\ell})$ such that

$$[A_1^\top, A_2^\top, \ldots, A_\ell^\top] \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_\ell \end{bmatrix} = 0 \quad \text{and} \quad b_1^\top y_1 + b_2^\top y_2 + \cdots + b_\ell^\top y_\ell \neq 0.$$

Since $\operatorname{ran}[A_1^\top, A_2^\top, \ldots, A_\ell^\top] = \operatorname{ran} A_1^\top \oplus \operatorname{ran} A_2^\top \oplus \cdots \oplus \operatorname{ran} A_\ell^\top$ holds by assumption, we have $A_r^\top y_r = 0$ for all $r \in \overline{1, \ell}$. Moreover, there exists an $r' \in \overline{1, \ell}$ such that $b_{r'}^\top y_{r'} \neq 0$. This contradicts the assumption, because then, by Proposition B.1, $\{x \in \mathbb{R}^n \mid A_{r'} x = b_{r'}\} = \emptyset$. $\square$

The next proposition is again a basic fact and hence we do not provide the proof of it here.

Proposition B.3 *Let U and V be finite dimensional vector spaces and let $A : U \to V$ be a linear map. Then* $\dim U = \dim \ker A + \operatorname{rank} A$.

As a consequence of Proposition B.3, we obtain the following proposition.

Proposition B.4 *Let n, c, and m be positive integers. Let $B \in \mathbb{R}^{n \times c}$ and $I \in \mathbb{R}^{c \times m}$. Then*

$$\dim \ker(B \cdot I) - \dim \ker I = \dim(\ker B \cap \operatorname{ran} I).$$

Proof Application of Proposition B.3 to the map $B|_{\operatorname{ran} I} : \operatorname{ran} I \to \mathbb{R}^c$ yields that

$$\operatorname{rank} I = \dim(\ker B \cap \operatorname{ran} I) + \operatorname{rank}(B|_{\operatorname{ran} I}).$$

Since $\operatorname{ran}(B|_{\operatorname{ran} I}) = \operatorname{ran}(B \cdot I)$, we have $\operatorname{rank}(B|_{\operatorname{ran} I}) = \operatorname{rank}(B \cdot I)$. Application of Proposition B.3 to both $B \cdot I : \mathbb{R}^m \to \mathbb{R}^n$ and $I : \mathbb{R}^m \to \mathbb{R}^c$ yields the desired result. $\square$

Appendix C

Analysis

We recall in Section C.1 the classical Implicit Function Theorem and in Section C.2 a multidimensional version of the Bolzano Theorem.

C.1 The Implicit Function Theorem

We recall the classical Implicit Function Theorem, because we use that in the proof of Proposition 5.4. For a proof, see e.g. [50, Theorem 9.28].

Theorem C.1 (The Implicit Function Theorem) *Let $U \subseteq \mathbb{R}^n \times \mathbb{R}^m$ be an open set and let $G : U \to \mathbb{R}^m$ be a continuously differentiable function. Assume also that $(a, b) \in U$ is such that $G(a, b) = 0$ and $(\partial_2 G)(a, b)$ is invertible. Then there exist an open neighbourhood V_a of a in $\mathbb{R}^n$ and an open neighbourhood V_b of b in $\mathbb{R}^m$ such that*

1. *$V_a \times V_b \subseteq U$ and*
2. *there exists a unique function $g : V_a \to V_b$ such that*
    (a) *$g(a) = b$,*
    (b) *$(x, g(x)) \in U$ for all $x \in V_a$, and*
    (c) *$G(x, g(x)) = 0$ for all $x \in V_a$.*

Moreover, the function g is continuously differentiable.

C.2 The Bolzano Theorem in $\mathbb{R}^n$

Since we use a multidimensional version of the Bolzano Theorem at the end of the proof of Theorem 5.2 in Section 5.3, we state and prove that in this section.

Theorem C.2 (The Bolzano Theorem in $\mathbb{R}^n$) *Let $f : [0,1]^n \to \mathbb{R}^n$ be a continuous function. Assume that for all $x \in \mathrm{bd}([0,1]^n)$ and for all $i \in \overline{1,n}$ we have*

$$f_i(x) \geq 0 \text{ if } x_i = 0 \text{ and}$$
$$f_i(x) \leq 0 \text{ if } x_i = 1.$$

Then there exists an $x^* \in [0,1]^n$ such that $f(x^*) = 0 \in \mathbb{R}^n$.

The main tool that we use to prove Theorem C.2 is the Brouwer Fixed Point Theorem (see [36, Chapter 5] or [44, Chapter 4]).

Theorem C.3 (The Brouwer Fixed Point Theorem) *Let $\widehat{F} : [0,1]^n \to [0,1]^n$ be a continuous function. Then there exists an $x^* \in [0,1]^n$ such that $\widehat{F}(x^*) = x^*$.*

Clearly, the existence of a zero for a function $f : [0,1]^n \to \mathbb{R}^n$ in Theorem C.2 is equivalent to the existence of a fixed point for $f + \mathrm{id}_{[0,1]^n}$, where $\mathrm{id}_{[0,1]^n}$ is the identity function on $[0,1]^n$. Therefore, Theorem C.2 above and Theorem C.4 below are equivalent. Thus, once we prove Theorem C.4, we obtain Theorem C.2 immediately.

Theorem C.4 *Let $F : [0,1]^n \to \mathbb{R}^n$ be a continuous function. Assume that for all $x \in \mathrm{bd}([0,1]^n)$ and for all $i \in \overline{1,n}$ we have*

$$F_i(x) \geq 0 \text{ if } x_i = 0 \text{ and}$$
$$F_i(x) \leq 1 \text{ if } x_i = 1.$$

Then there exists an $x^* \in [0,1]^n$ such that $F(x^*) = x^*$.

Proof Let us define the function $\widehat{F} : [0,1]^n \to [0,1]^n$ by defining its ith coordinate function by

$$\widehat{F}_i = \max(\min(F_i, 1), 0) \quad (i \in \overline{1,n}).$$

We first show that the fixed point sets of F and $\widehat{F}$ coincide. First, let $x \in [0,1]^n$ be such that $F(x) = x$. Since $\max(\min(\alpha, 1), 0) = \alpha$ for all $\alpha \in [0,1]$, we have $\widehat{F}(x) = x$. Conversely, let $x \in [0,1]^n$ be such that $\widehat{F}(x) = x$. If $i \in \overline{1,n}$ is such that $0 < x_i < 1$ then $0 < \widehat{F}_i(x) < 1$. Consequently, $\widehat{F}_i(x) = F_i(x)$. If $i \in \overline{1,n}$ is such that $x_i = 0$ then $\widehat{F}_i(x) = 0$. Therefore, $F_i(x) \leq 0$. Since $F_i(x) \geq 0$ by assumption, we obtain that $F_i(x) = 0$, or equivalently, $\widehat{F}_i(x) = F_i(x)$. Similar argument shows that if $i \in \overline{1,n}$ is such that $x_i = 1$ then $\widehat{F}_i(x) = F_i(x)$ follows. Hence, the fixed point sets of F and $\widehat{F}$ indeed coincide.

Clearly, $\widehat{F}$ is continuous and therefore Theorem C.3 implies that $\widehat{F}$ has a fixed point. It follows then that F also has a fixed point. □

To serve better our purposes in Section 5.3, we conclude this section by stating an obvious generalisation of Theorem C.2.

Theorem C.5 *Let $b_1, \ldots, b_n$ be positive real numbers and let $f : \times_{i=1}^{n}[0, b_i] \to \mathbb{R}^n$ be a continuous function. Assume that for all $x \in \mathrm{bd}(\times_{i=1}^{n}[0, b_i])$ and for all $i \in \overline{1, n}$ we have*

$$\begin{aligned} &f_i(x) \geq 0 \text{ if } x_i = 0 \text{ and} \\ &f_i(x) \leq 0 \text{ if } x_i = b_i. \end{aligned} \tag{C.1}$$

Then there exists an $x^* \in \times_{i=1}^{n}[0, b_i]$ such that $f(x^*) = 0 \in \mathbb{R}^n$.

We have depicted (C.1) in the two-dimensional case in Figure C.1.

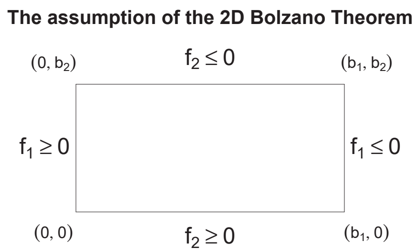


Figure C.1: The assumptions on the signs of the coordinate functions of the continuous function $f : [0, b_1] \times [0, b_2] \to \mathbb{R}^2$ in the two-dimensional case of the Bolzano Theorem (see Theorem C.5).

Appendix D

The Matrix-Tree Theorem

There are several versions of the Matrix-Tree Theorem. The one we present in Section D.2 appears in [47, Appendix] as a tool for proving the Markov Chain Tree Theorem. This is a slight generalisation of Tutte's result (see [56, Theorem 3.6]), while it is a special case of the All Minors Matrix Tree Theorem (see [15]). The previous applications of the Matrix-Tree Theorem in CRNT used Tutte's version (see [17, 24, 33, 34, 46, 55]), while we need a slightly more general variation in Section 6.3. We also provide a direct and elementary proof of the Matrix-Tree Theorem in Section D.2, which was worked out by György Michaletzky and the author of this thesis.

D.1 A lemma on the number of inversions in bijections

In the proof of the Matrix-Tree Theorem, we use a purely algebraic lemma, which is a special case of a result in [15]. For the sake of completeness, we also present the proof of this lemma.

Fix a positive integer n for this section. Let W_1 and W_2 be nonempty subsets of $V = \{1, \ldots, n\}$ such that $|W_1| = |W_2|$. For a bijection $\pi : W_1 \to W_2$, we say that $k \in W_1$ and $k' \in W_1$ are in *inversion* if $k < k'$ and $\pi(k) > \pi(k')$. Denote by $\nu(\pi)$ the *number of inversions* in π, i.e.,

$$\nu(\pi) = |\{(k, k') \in W_1 \times W_1 \mid k < k' \text{ and } \pi(k) > \pi(k')\}|.$$

As usual, define the *sign* of the bijection π by $\operatorname{sgn}(\pi) = (-1)^{\nu(\pi)}$.

Lemma D.1 *Let $i, j \in V$. Let $\sigma : V\backslash\{j\} \to V\backslash\{i\}$ be a bijection and define the permutation $\overline{\sigma} : V \to V$ by*

$$\overline{\sigma}(k) = \begin{cases} \sigma(k), & \text{if } k \in V\backslash\{j\}, \\ i, & \text{if } k = j. \end{cases}$$

Then $\operatorname{sgn}(\overline{\sigma}) = (-1)^{i+j}\operatorname{sgn}(\sigma)$.

Proof We prove this lemma by induction on j. To prove the initial step of the induction, let $j = 1$. Clearly, $\overline{\sigma}$ inherits all the inversions of σ. Also, since $\overline{\sigma}(1) = i$, there are exactly $i - 1$

elements in $V\backslash\{1\}$ that are in inversion with 1 under $\overline{\sigma}$. Hence, $\nu(\overline{\sigma}) = \nu(\sigma) + (i-1)$. As a consequence,

$$\operatorname{sgn}(\overline{\sigma}) = (-1)^{\nu(\overline{\sigma})} = (-1)^{\nu(\sigma)+(i-1)} = (-1)^{i-1}(-1)^{\nu(\sigma)} = (-1)^{i+1}\operatorname{sgn}(\sigma).$$

To prove the inductive step, fix $2 \leq j \leq n$ and assume that the lemma holds with $j-1$ instead of j. Let us define $\pi : V\backslash\{j-1\} \to V\backslash\{i\}$ by

$$\pi(k) = \begin{cases} \sigma(k), & \text{if } k \in V\backslash\{j-1, j\}, \\ \sigma(j-1), & \text{if } k = j. \end{cases}$$

Clearly, we have $\nu(\pi) = \nu(\sigma)$. Also, let us define $\overline{\pi} : V \to V$ by

$$\overline{\pi}(k) = \begin{cases} \pi(k), & \text{if } k \in V\backslash\{j-1\}, \\ i, & \text{if } k = j-1. \end{cases}$$

Note that we have defined $\overline{\pi}$ in such a way that $\overline{\pi}|_{V\backslash\{j-1,j\}} = \overline{\sigma}|_{V\backslash\{j-1,j\}}$, $\overline{\pi}(j) = \overline{\sigma}(j-1)$, and $\overline{\pi}(j-1) = \overline{\sigma}(j) = i$. Thus, for $k, k' \in V$ such that $k < k'$ we have

$$\overline{\pi}(k) > \overline{\pi}(k') \text{ if and only if } \begin{cases} \overline{\sigma}(k) > \overline{\sigma}(k'), & \text{if } k, k' \in V\backslash\{j-1, j\}, \\ \overline{\sigma}(k) > \overline{\sigma}(j-1), & \text{if } k \in \{1, \ldots, j-2\}, k' = j, \\ \overline{\sigma}(k) > \overline{\sigma}(j), & \text{if } k \in \{1, \ldots, j-2\}, k' = j-1, \\ \overline{\sigma}(j-1) > \overline{\sigma}(k'), & \text{if } k = j, k' \in \{j+1, \ldots, n\}, \\ \overline{\sigma}(j) > \overline{\sigma}(k'), & \text{if } k = j-1, k'\{j+1, \ldots, n\}, \text{ and} \\ \overline{\sigma}(j-1) < \overline{\sigma}(j), & \text{if } k = j-1, k' = j. \end{cases}$$

Hence,

$$\nu(\overline{\pi}) = \begin{cases} \nu(\overline{\sigma}) + 1, & \text{if } \overline{\sigma}(j-1) < \overline{\sigma}(j), \\ \nu(\overline{\sigma}) - 1, & \text{if } \overline{\sigma}(j-1) > \overline{\sigma}(j). \end{cases} \tag{D.1}$$

Therefore,

$$\operatorname{sgn}(\overline{\sigma}) = (-1)^{\nu(\overline{\sigma})} \overset{(D.1)}{=} -(-1)^{\nu(\overline{\pi})} = -(-1)^{i+(j-1)}\operatorname{sgn}(\pi) = (-1)^{i+j}\operatorname{sgn}(\sigma),$$

where we used the inductive hypothesis for $\overline{\pi}$. This concludes the proof. □

The following corollary is a direct consequence of Lemma D.1.

Corollary D.2 *Let $Q \subseteq V$ and $i, j \in V\backslash Q$. Let $\sigma : V\backslash(Q \cup \{j\}) \to V\backslash(Q \cup \{i\})$ be a bijection and define the permutation $\overline{\sigma} : V\backslash Q \to V\backslash Q$ by*

$$\overline{\sigma}(k) = \begin{cases} \sigma(k), & \text{if } k \in V\backslash(Q \cup \{j\}), \\ i, & \text{if } k = j. \end{cases}$$

Then $\operatorname{sgn}(\overline{\sigma}) = (-1)^{i+j}\operatorname{sgn}(\sigma)$.

D.2 The Matrix-Tree Theorem

Fix a positive integer n for this section. Associate to a matrix $Z = (z_{ij})_{i,j=1}^n \in \mathbb{R}^{n\times n}$ the directed graph $D(Z) = (V(Z), A(Z))$, where $V(Z) = \{1, \ldots, n\}$ and $A(Z) = \{(i, j) \in V(Z)\times V(Z) \mid z_{ij} \neq 0\}$. Also, for $Q_1, Q_2 \subseteq \{1, \ldots, n\}$ with $|Q_1| = |Q_2|$, denote by $d_{Q_1,Q_2}(Z)$ the determinant of that matrix, which is obtained from Z by deleting the rows with index in Q_1 and the columns with index in Q_2.

Theorem D.3 (Matrix-Tree Theorem) *Let $Z = (z_{ij})_{i,j=1}^n \in \mathbb{R}^{n\times n}$ be a matrix that satisfy*

$$\sum_{j=1}^{n} z_{ij} = 0 \textit{ for all } i \in \{1, \ldots, n\}. \tag{D.2}$$

Fix $Q \subseteq \{1, \ldots, n\}$ and $i, j \in \{1, \ldots, n\}\backslash Q$. Then

$$d_{Q\cup\{j\},Q\cup\{i\}}(Z) = (-1)^{i+j}(-1)^{n-|Q|-1} \sum_{\widetilde{A}\in\mathcal{T}^{ij}_{D(Z)}(Q\cup\{j\})} z_{\widetilde{A}},$$

where $\mathcal{T}^{ij}_{D(Z)}(Q \cup \{j\})$ is understood as in (A.3) *and the symbol $z_{\widetilde{A}}$ is a shorthand notation for the product $\prod_{a\in\widetilde{A}} z_a$.*

Proof For shorthand notation, let us denote by S_{ij} the set of bijections from $V\backslash(Q \cup \{j\})$ to $V\backslash(Q \cup \{i\})$. For an element σ of S_{ij}, denote by $\overline{\sigma}$ the permutation of $V\backslash Q$, which is defined by

$$\overline{\sigma}(k) = \begin{cases} \sigma(k), & \text{if } k \in V\backslash(Q \cup \{j\}), \\ i, & \text{if } k = j. \end{cases}$$

Since $\overline{\sigma}$ is a permutation, we may consider its decomposition into disjoint cyclic permutations. This also yields a decomposition of σ into cyclic permutations and a "path bijection" from i to j, where the "path bijection" comes from the "deletion" of the assignment $j \mapsto i$ from $\overline{\sigma}$. Denote by

h^σ the "path bijection" component of σ,

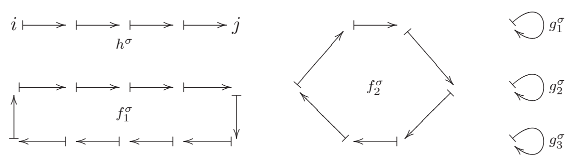
p_σ the number of cycles of σ of length at least 2,

$f_1^\sigma, \ldots, f_{p_\sigma}^\sigma$ the cycles of σ of length at least 2,

q_σ the number of cycles of σ of length 1, and

$g_1^\sigma, \ldots, g_{q_\sigma}^\sigma$ the cycles of σ of length 1.

See (D.3) for an illustration of this decomposition. For this specific example, we have $p_\sigma = 2$ and $q_\sigma = 3$.



(D.3)

For notational convenience, we denote by z_{h^σ} and $z_{f_l^\sigma}$ the product of those entries of Z that correspond to the arcs of the directed path h^σ and the directed circuit f_l^σ, respectively. (Thus, we implicitly identify the bijections h^σ and f_l^σ with the corresponding directed path and directed circuit, respectively.) Also, we identify g_l^σ with the respective vertex, and thus $z_{g_l^\sigma, g_l^\sigma}$ is the corresponding diagonal entry of Z. Then

$$\begin{aligned}
d_{Q\cup\{j\},Q\cup\{i\}}(Z) &= \sum_{\sigma\in S_{ij}} \left[\operatorname{sgn}(\sigma)\cdot\left(\prod_{k\in V\setminus(Q\cup\{j\})} z_{k,\sigma(k)}\right)\right] = \\
&= \sum_{\sigma\in S_{ij}} \left[\operatorname{sgn}(\sigma)\cdot z_{h^\sigma}\cdot\left(\prod_{l=1}^{p_\sigma} z_{f_l^\sigma}\right)\cdot\left(\prod_{l=1}^{q_\sigma} z_{g_l^\sigma,g_l^\sigma}\right)\right] \overset{(D.2)}{=} \\
&\overset{(D.2)}{=} \sum_{\sigma\in S_{ij}} \left[\operatorname{sgn}(\sigma)\cdot z_{h^\sigma}\cdot\left(\prod_{l=1}^{p_\sigma} z_{f_l^\sigma}\right)\cdot\left(\prod_{l=1}^{q_\sigma}\left\{-\sum_{k\in V\setminus\{g_l^\sigma\}} z_{g_l^\sigma,k}\right\}\right)\right] = \\
&= \sum_{\sigma\in S_{ij}} \left[\operatorname{sgn}(\sigma)\cdot(-1)^{q_\sigma}\cdot\left(\sum_{\widetilde{A}\in\mathcal{A}^{ij,\sigma}_{D(Z)}(Q\cup\{j\})} z_{\widetilde{A}}\right)\right] = \\
&= \sum_{\widetilde{A}\in\mathcal{A}^{ij}_{D(Z)}(Q\cup\{j\})} z_{\widetilde{A}} \left[\sum_{\substack{\sigma\in S_{ij}\\ h^\sigma=h^{\widetilde{A}}\\ f_1^\sigma,\ldots,f_{p_\sigma}^\sigma\subseteq\widetilde{A}}} \operatorname{sgn}(\sigma)\cdot(-1)^{q_\sigma}\right],
\end{aligned}$$

where $h^{\widetilde{A}}$ is the unique directed path from i to j in $(V,\widetilde{A})$ and

$$\mathcal{A}^{ij,\sigma}_{D(Z)}(Q\cup\{j\}) = \left\{\widetilde{A}\in\mathcal{A}^{ij}_{D(Z)}(Q\cup\{j\}) \;\middle|\; \begin{array}{l} f_1^\sigma,\ldots,f_{p_\sigma}^\sigma\subseteq\widetilde{A} \text{ and the unique directed} \\ \text{path from } i \text{ to } j \text{ in } (V,\widetilde{A}) \text{ is given by } h^\sigma \end{array}\right\}$$

(recall (A.2)). Fix $\widetilde{A}\in\mathcal{A}^{ij}_{D(Z)}(Q\cup\{j\})$ for the rest of this proof. We claim that

$$\sum_{\substack{\sigma\in S_{ij}\\ h^\sigma=h^{\widetilde{A}}\\ f_1^\sigma,\ldots,f_{p_\sigma}^\sigma\subseteq\widetilde{A}}} \operatorname{sgn}(\sigma)\cdot(-1)^{q_\sigma} = \begin{cases} 0, & \text{if } \widetilde{A}\notin\mathcal{T}^{ij}_{D(Z)}(Q\cup\{j\}),\\ (-1)^{i+j}(-1)^{n-|Q|-1}, & \text{if } \widetilde{A}\in\mathcal{T}^{ij}_{D(Z)}(Q\cup\{j\}). \end{cases} \tag{D.4}$$

By Corollary D.2,

$$\operatorname{sgn}(\sigma) = (-1)^{i+j}\operatorname{sgn}(\overline{\sigma}) = (-1)^{i+j}(-1)^{\operatorname{len}(h^\sigma)}(-1)^{\sum_{l=1}^{p_\sigma}(\operatorname{len}(f_l^\sigma)-1)} = (-1)^{i+j}(-1)^{n-|Q|-1-p_\sigma-q_\sigma}. \tag{D.5}$$

Thus, $\operatorname{sgn}(\sigma)\cdot(-1)^{q_\sigma} = (-1)^{i+j}(-1)^{n-|Q|-1-p_\sigma}$, which depends on σ only through p_σ.

If $\widetilde{A}\in\mathcal{T}^{ij}_{D(Z)}(Q\cup\{j\})$ (i.e., $\widetilde{A}$ is acyclic) then the sum on the left hand side of (D.4) contains only one term (there is only one element $\sigma\in S_{ij}$ for which $h^\sigma = h^{\widetilde{A}}$ and $p_\sigma = 0$). Thus, by (D.5), we obtain (D.4) for the case $\widetilde{A}\in\mathcal{T}^{ij}_{D(Z)}(Q\cup\{j\})$.

Assume for the rest of this proof that $\widetilde{A} \notin \mathcal{T}^{ij}_{D(Z)}(Q \cup \{j\})$. Denote by m the number of directed circuits in $\widetilde{A}$. Since $\widetilde{A} \notin \mathcal{T}^{ij}_{D(Z)}(Q \cup \{j\})$, we have $m \geq 1$. With this and (D.5), we have

$$\begin{aligned}\sum_{\substack{\sigma \in S_{ij} \\ h^\sigma = h^{\widetilde{A}} \\ f_1^\sigma, \dots, f_{p_\sigma}^\sigma \subseteq \widetilde{A}}} \operatorname{sgn}(\sigma) \cdot (-1)^{q_\sigma} &= (-1)^{i+j}(-1)^{n-|Q|-1} \cdot \sum_{\substack{\sigma \in S_{ij} \\ h^\sigma = h^{\widetilde{A}} \\ f_1^\sigma, \dots, f_{p_\sigma}^\sigma \subseteq \widetilde{A}}} (-1)^{p_\sigma} = \\ &= (-1)^{i+j}(-1)^{n-|Q|-1} \cdot \sum_{k=0}^{m} \binom{m}{k} (-1)^k = 0,\end{aligned}$$

where the last equality follows from the Binomial Theorem. $\square$

Bibliography

[1] D.F. Anderson. Global asymptotic stability for a class of nonlinear chemical equations. *SIAM J. Appl. Math.*, 68(5):1464–1476, 2008.

[2] D.F. Anderson. Boundedness of trajectories for weakly reversible, single linkage class reaction systems. *Journal of Mathematical Chemistry*, 49:2275–2290, 2011. 10.1007/s10910-011-9886-4.

[3] D.F. Anderson. A proof of the global attractor conjecture in the single linkage class case. *SIAM J. Appl. Math.*, 71(4):1487–1508, 2011.

[4] D.F. Anderson and A. Shiu. The dynamics of weakly reversible population processes near facets. *SIAM J. Appl. Math.*, 70(6):1840–1858, 2010.

[5] D. Angeli, P. De Leenheer, and E.D. Sontag. A Petri net approach to the study of persistence in chemical reaction networks. *Math. Biosci.*, 210(2):598–618, 2007.

[6] D. Angeli, P. De Leenheer, and E.D. Sontag. Persistence results for chemical reaction networks with time-dependent kinetics and no global conservation laws. *SIAM J. Appl. Math.*, 71(1):128–146, 2011.

[7] M. Banaji and G. Craciun. Graph-theoretic criteria for injectivity and unique equilibria in general chemical reaction systems. *Adv. in Appl. Math.*, 44(2):168–184, 2010.

[8] M. Banaji, P. Donnell, and S. Baigent. P matrix properties, injectivity, and stability in chemical reaction systems. *SIAM J. Appl. Math.*, 67(6):1523–1547, 2007.

[9] J. Bang-Jensen and G. Gutin. *Digraphs*. Springer Monographs in Mathematics. Springer-Verlag London Ltd., London, second edition, 2009. Theory, algorithms and applications.

[10] B. Boros. Dynamic system properties of biochemical reaction systems. Master's thesis, Vrije Universiteit, Amsterdam and Eötvös Loránd University, Budapest, May 2008. Available at `http://www.cs.elte.hu/~bboros/BBorosMasterThesis.pdf`.

[11] B. Boros. Notes on the Deficieny One Theorem: single linkage class. In A. Edelmayer, editor, *Proceedings of the 19th International Symposium on Mathematical Theory of Networks and Systems*, pages 1953–1960, July 2010.

[12] B. Boros. Notes on the Deficieny-One Theorem: multiple linkage classes. *Math. Biosci.*, 235(1):110–122, 2012.

[13] B. Boros. On the dependence of the existence of the positive steady states on the rate coefficients for deficiency-one mass action systems: single linkage class. *J. Math. Chem.*, 2013. DOI: 10.1007/s10910-013-0222-z.

[14] B. Boros. On the existence of the positive steady states of weakly reversible deficiency-one mass action systems. *Math. Biosci.*, 2013. DOI: 10.1016/j.mbs.2013.06.006.

[15] S. Chaiken. A combinatorial proof of the all minors matrix tree theorem. *SIAM J. Algebraic Discrete Methods*, 3(3):319–329, 1982.

[16] M. Chaves. *Observer design for a class of nonlinear systems, with applications to biochemical networks*. ProQuest LLC, Ann Arbor, MI, 2003. Thesis (Ph.D.)–Rutgers The State University of New Jersey - New Brunswick.

[17] G. Craciun, A. Dickenstein, A. Shiu, and B. Sturmfels. Toric dynamical systems. *J. Symb. Comput.*, 44(11):1551–1565, 2009.

[18] G. Craciun and M. Feinberg. Multiple equilibria in complex chemical reaction networks. I. The injectivity property. *SIAM J. Appl. Math.*, 65(5):1526–1546 (electronic), 2005.

[19] G. Craciun and M. Feinberg. Multiple equilibria in complex chemical reaction networks. II. The species-reaction graph. *SIAM J. Appl. Math.*, 66(4):1321–1338 (electronic), 2006.

[20] G. Craciun and M. Feinberg. Multiple equilibria in complex chemical reaction networks: semiopen mass action systems. *SIAM J. Appl. Math.*, 70(6):1859–1877, 2010.

[21] G. Craciun, J.W. Helton, and R.J. Williams. Homotopy methods for counting reaction network equilibria. *Math. Biosci.*, 216(2):140–149, 2008.

[22] G. Craciun, F. Nazarov, and C. Pantea. Persistence and Permanence of Mass-Action and Power-Law Dynamical Systems. *SIAM J. Appl. Math.*, 73(1):305–329, 2013.

[23] J. Deng, M. Feinberg, C. Jones, and A. Nachman. On the steady states of weakly reversible chemical reaction networks. Available at `http://arxiv.org/pdf/1111.2386v2.pdf`, 2011.

[24] A. Dickenstein and M. Pérez Millán. How far is complex balancing from detailed balancing? *Bull. Math. Biol.*, 73(4):811–828, 2011.

[25] M. Feinberg. Lectures on chemical reaction networks. 4.5 out of 9 lectures delivered at the Mathematics Research Center, University of Wisconsin, Fall 1979. Available at `http://www.che.eng.ohio-state.edu/~feinberg/LecturesOnReactionNetworks`.

[26] M. Feinberg. Complex balancing in general kinetic systems. *Arch. Rational Mech. Anal.*, 49:187–194, 1972/73.

[27] M. Feinberg. Chemical reaction network structure and the stability of complex isothermal reactors - I. The Deficiency Zero and the Deficiency One Theorems. *Chemical Engineering Science*, 42(10):2229–2268, 1987.

[28] M. Feinberg. Chemical reaction network structure and the stability of complex isothermal reactors - II. Multiple steady states for networks of deficiency one. *Chemical Engineering Science*, 43(1):1 – 25, 1988.

[29] M. Feinberg. The existence and uniqueness of steady states for a class of chemical reaction networks. *Arch. Rational Mech. Anal.*, 132(4):311–370, 1995.

[30] M. Feinberg. Multiple steady states for chemical reaction networks of deficiency one. *Arch. Rational Mech. Anal.*, 132(4):371–406, 1995.

[31] M. Feinberg and F. Horn. Dynamics of open chemical systems and the algebraic structure of the underlying reaction network. *Chemical Engineering Science*, 29(3):775 – 787, 1974.

[32] M. Feinberg and F. Horn. Chemical mechanism structure and the coincidence of the stoichiometric and kinetic subspaces. *Arch. Rational Mech. Anal.*, 66(1):83–97, 1977.

[33] E. Feliu and C. Wiuf. Variable elimination in chemical reaction networks with mass-action kinetics. *SIAM J. Appl. Math.*, 72(4):959–981, 2012.

[34] E. Feliu and C. Wiuf. Variable elimination in post-translational modification reaction networks with mass-action kinetics. *J. Math. Biol.*, 66(1-2):281–310, 2013.

[35] L. Georgiadis, R.E. Tarjan, and R.F. Werneck. Finding dominators in practice. *J. Graph Algorithms Appl.*, 10(1):69–94, 2006.

[36] A. Granas and J. Dugundji. *Fixed Point Theory*. Springer Monographs in Mathematics. Springer, 2003.

[37] P. Gray and S.K. Scott. Autocatalytic reactions in the isothermal, continuous stirred tank reactor: Isolas and other forms of multistability. *Chemical Engineering Science*, 38(1):29 – 43, 1983.

[38] F. Horn. Necessary and sufficient conditions for complex balancing in chemical kinetics. *Arch. Rational Mech. Anal.*, 49:172–186, 1972/73.

[39] F. Horn. On a connexion between stability and graphs in chemical kinetics. I. Stability and the reaction diagram. *Proc. Roy. Soc. (London) Ser. A*, 334:299–312, 1973.

[40] F. Horn. On a connexion between stability and graphs in chemical kinetics. II. Stability and the complex graph. *Proc. Roy. Soc. (London) Ser. A*, 334:313–330, 1973.

[41] F. Horn. Stability and complex balancing in mass-action systems with three short complexes. *Proc. Roy. Soc. (London) Ser. A*, 334:331–342, 1973.

[42] F. Horn. The dynamics of open reaction systems. In *Mathematical aspects of chemical and biochemical problems and quantum chemistry (Proc. SIAM-AMS Sympos. Appl. Math., New York, 1974)*, pages 125–137. SIAM–AMS Proceedings, Vol. VIII. Amer. Math. Soc., Providence, R.I., 1974.

[43] F. Horn and R. Jackson. General mass action kinetics. *Arch. Rational Mech. Anal.*, 47:81–116, 1972.

[44] V.I. Istratescu. *Fixed Point Theory: An Introduction*. Mathematics and Its Applications. Springer, 2002.

[45] M.D. Johnston and D. Siegel. Weak dynamical nonemptiability and persistence of chemical kinetics systems. *SIAM J. Appl. Math.*, 71(4):1263–1279, 2011.

[46] R.L. Karp, M. Pérez Millán, T. Dasgupta, A. Dickenstein, and J. Gunawardena. Complex-linear invariants of biochemical networks. *J. Theoret. Biol.*, 311:130–138, 2012.

[47] F.T. Leighton and R.L. Rivest. Estimating a probability using finite memory. In *Foundations of computation theory (Borgholm, 1983)*, volume 158 of *Lecture Notes in Comput. Sci.*, pages 255–269. Springer, Berlin, 1983.

[48] V.N. Orlov and L.I. Rozonoèr. The macrodynamics of open systems and the variational principle of the local potential. II. Applications. *J. Franklin Inst.*, 318(5):315–347, 1984.

[49] C. Pantea. On the persistence and global stability of mass-action systems. *SIAM J. Math. Anal.*, 44(3):1636–1673, 2012.

[50] W. Rudin. *Principles of mathematical analysis*. McGraw-Hill Book Co., New York, third edition, 1976. International Series in Pure and Applied Mathematics.

[51] A. Schrijver. *Combinatorial optimization. Polyhedra and efficiency. Vol. A*, volume 24 of *Algorithms and Combinatorics*. Springer-Verlag, Berlin, 2003. Paths, flows, matchings, Chapters 1–38.

[52] G. Shinar and M. Feinberg. Structural sources of robustness in biochemical reaction networks. *Science*, 327(5971):1389–1391, March 2010.

[53] P.L. Simon. Globally attracting domains in two-dimensional reversible chemical dynamical systems. *Ann. Univ. Sci. Budapest. Sect. Comput.*, 15:179–200, 1995.

[54] E.D. Sontag. Structure and stability of certain chemical networks and applications to the kinetic proofreading model of T-cell receptor signal transduction. *IEEE Trans. Automat. Control*, 46(7):1028–1047, 2001.

[55] M. Thomson and J. Gunawardena. The rational parameterisation theorem for multisite post-translational modification systems. *J. Theoret. Biol.*, 261(4):626–636, 2009.

[56] W.T. Tutte. The dissection of equilateral triangles into equilateral triangles. *Proc. Cambridge Philos. Soc.*, 44:463–482, 1948.

[57] A.I. Vol′pert. Differential equations on graphs. *Mat. Sb. (N.S.)*, 88(130):578–588, 1972.

[58] A.I. Vol′pert and S.I. Hudjaev. *Analysis in classes of discontinuous functions and equations of mathematical physics*, volume 8 of *Mechanics: Analysis*. Martinus Nijhoff Publishers, Dordrecht, 1985.

Summary

The foundations of Chemical Reaction Network Theory, which aims at the investigation of the mathematical models of chemical and biological systems, was developed by Feinberg, Horn, and Jackson in the 1970's. The purpose of this thesis is to revisit and improve the *deficiency-oriented* theory of mass action systems. The classical Deficiency-Zero- and Deficiency-One Theorems answer questions about the existence, uniqueness, and stability properties of the positive steady states. The main goal of this thesis is to investigate the existence of positive steady states of such deficiency-one mass action systems for which this question is not answered by the Deficiency-One Theorem.

The Deficiency-One Theorem states that there exists a unique positive steady state in each positive stoichiometric class for every weakly reversible deficiency-one mass action systems with single linkage class (regardless of the values of the rate coefficients). Under the extra assumption that the set of positive steady states is nonempty, the previous statement remains valid even if we omit the weak reversibility. However, the question of the non-emptiness of the set of positive steady states in the non weakly reversible case has not been addressed so far. In this thesis, we show that a trivially obtained necessary condition also serves as a sufficient condition to the non-emptiness of the set of positive steady states. Thus, we make the Deficiency-One Theorem complete in respect of the existence of the positive steady states. The obtained equivalent condition involves the rate coefficients. This raises the natural question of whether we can characterise those reaction networks for which the associated mass action system has nonempty set of positive steady states *for any* choice of rate coefficients. Using more involved graph theoretical arguments, we provide such a characterisation.

As a generalisation of the Deficiency-One Theorem to another direction, we prove the existence of a positive steady state in each positive stoichiometric class for every weakly reversible deficiency-one mass action systems with multiple linkage classes (regardless of the values of the rate coefficients). It turned out that independently of our work, Deng, Feinberg, Jones, and Nachman obtained the same conclusion without any assumption on the deficiency. Thus, their (yet unpublished) result is substantially more general. The proof by Deng et al. owes more to geometric ideas while our work uses more strictly algebraic methods. Most of the intermediate results of Deng et al. rely heavily on the weak reversibility of the network, while in our reasoning the weak reversibility of the network becomes crucial only in the concluding steps. Rather, we take advantage of the fact that the deficiency of the network is assumed to be one.

Összefoglalás (in Hungarian)

A kémiai reakcióhálózatok elméletének alapjait Feinberg, Horn és Jackson fektették le az 1970-es években. Az elmélet kémiai és biológia rendszerek matematikai modelljének vizsgálatával foglalkozik. Az értekezés célja, hogy bemutassuk és továbbfejlesszük a tömeghatás kinetikájú rendszerek *deficiencia-orientált* eredményeit. A klasszikus 0- és 1-*Deficiencia Tételek* a rendszer pozitív egyensúlyi pontjainak létezésével, egyértelműségével és stabilitásával foglalkoznak. Fő célkitűzésünk olyan 1-deficienciájú tömeghatás kinetikájú rendszerek pozitív egyensúlyi pontjainak létezését vizsgálni, melyek nem teljesítik az 1-Deficiencia Tétel feltételeit.

Az 1-Deficiencia Tétel szerint minden egyetlen láncosztállyal rendelkező gyengén megfordítható 1-deficienciájú tömeghatás kinetikájú rendszernek pontosan egy pozitív egyensúlyi pontja van minden pozitív sztöchiometriai osztályában (függetlenül a sebességi együtthatók értékeitől). Ha elhagyjuk a gyenge megfordíthatóságot, viszont feltesszük, hogy létezik pozitív egyensúlyi pont, akkor az előző tétel következtetése érvényben marad. Azonban a nem gyengén megfordítható esetben a pozitív egyensúlyi pontok létezésével kapcsolatban korábban nem születtek eredmények. Az értekezésben megmutatjuk, hogy a pozitív egyensúlyi pontok létezéséhez egy triviálisan adódó szükséges feltétel egyúttal elégséges is. Ezzel teljessé tesszük az 1-Deficiencia Tételt a pozitív egyensúlyi pontok létezése tekintetében. A kapott ekvivalens feltételben szerepelnek a sebességi együtthatók, így természetes módon vetődik fel az igény, hogy karakterizáljuk azon reakcióhálózatokat, melyek esetén a pozitív egyensúlyi pontok létezése nem függ a hálózathoz rendelt sebességi együtthatók értékeitől. Összetettebb gráfelméleti gondolatmenetek felhasználásával bemutatunk egy ilyen karakterizációt az értekezésben.

Az 1-Deficiencia Tétel más irányú általánosításaként megmutatjuk, hogy minden több láncosztállyal rendelkező gyengén megfordítható 1-deficienciájú tömeghatás kinetikájú rendszernek létezik pozitív egyensúlyi pontja minden pozitív sztöchiometriai osztályában (függetlenül a sebességi együtthatók értékeitől). Időközben kiderült, hogy tőlünk függetlenül Deng, Feinberg, Jones és Nachman ugyanerre a következtetésre jutott, ők azonban nem tételeztek fel semmit a deficienciáról. Így az ő (egyelőre nem publikált) eredményük lényegesen általánosabb a mienknél. Deng és mtsai. geometriai eszközöket használnak, míg mi főképpen algebrai módszereket alkalmazunk. A Deng és mtsai. által bemutatott gondolatmenet legtöbb közbülső eredményénél lényegesen szerepe van a gyenge megfordíthatóságnak, míg a mi bizonyításunkban ez csak a záró lépések során válik fontossá. Nálunk inkább a deficienciáról tett megkötés játssza az alapvető szerepet.